



# **STIC Search Report**

## **Biotech-Chem Library**

**STIC Database Tracking Number: 100887**

**TO: Jennifer Kim**  
**Location: cm1/2b19/2d17**  
**Art Unit: 1617**  
**Wednesday, August 13, 2003**

**Case Serial Number: 10073607**

**From: Toby Port**  
**Location: Biotech-Chem Library**  
**CM1-6A04**  
**Phone: 308-3534**

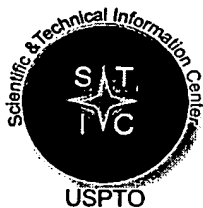
**[toby.port@uspto.gov](mailto:toby.port@uspto.gov)**

### **Search Notes**

Dear Examiner Kim,

Here are the results of your search.  
Please feel free to contact me if you have any questions.

Toby Port



# STIC SEARCH RESULTS FEEDBACK FORM

## Biotech-Chem Library

Questions about the scope or the results of the search? Contact *the searcher or contact:*

Mary Hale, Information Branch Supervisor  
308-4258, CM1-1E01

## Voluntary Results Feedback Form

➤ I am an examiner in Workgroup:  Example: 1610

➤ Relevant prior art **found**, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature  
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art **not found**:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library CM1 – Circ. Desk



Toby Part 100887

Access DB# \_\_\_\_\_

# SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jennifer Kim Examiner #: 77469 Date: 8/12/03  
Art Unit: 1619 Phone Number 308-2232 Serial Number: 10/073607  
Mail Box and Bldg/Room Location: 2D17 Results Format Preferred (circle): PAPER DISK E-MAIL  
2B19

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*  
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Methods + Compositions for the treatment of alopecia + other disorders of the pilosebaceous apparatus  
Inventors (please provide full names): Krajcik et al.

Earliest Priority Filing Date: 2/23/2000

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search claims 1-8 + 13-19 based on  
the active agent of a biguanide (e.g. metformin  
phenformin  
buformin)

PMX,

jr

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## STAFF USE ONLY

### Type of Search

### Vendors and cost where applicable

Searcher: \_\_\_\_\_ NA Sequence (#) \_\_\_\_\_ STN: \_\_\_\_\_

Searcher Phone #: \_\_\_\_\_ AA Sequence (#) \_\_\_\_\_ Dialog: \_\_\_\_\_

=> file reg

FILE 'REGISTRY' ENTERED AT 14:29:07 ON 12 AUG 2003  
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STRUCTURE FILE UPDATES: 11 AUG 2003 HIGHEST RN 565156-77-6  
DICTIONARY FILE UPDATES: 11 AUG 2003 HIGHEST RN 565156-77-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNnote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d rn cn l3

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 657-24-9 REGISTRY  
CN Imidodicarbonimidic diamide, N,N-dimethyl- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Biguanide, 1,1-dimethyl- (6CI, 8CI)  
OTHER NAMES:  
CN 1,1-Dimethylbiguanide  
CN Dimethylbiguanide  
CN DMGG  
CN Fluamine  
CN Flumamine  
CN Gliguanid  
CN Haurymelin  
CN Melbin  
CN **Metformin**  
CN Metiguanide  
CN N'-Dimethylguanylguanidine  
CN N,N-Dimethylbiguanide  
CN N,N-Dimethyldiguanide  
CN N1,N1-Dimethylbiguanide  
CN NNDG  
CN Siofor

=> d rn cn l4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 114-86-3 REGISTRY  
CN Imidodicarbonimidic diamide, N-(2-phenylethyl)- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Biguanide, 1-phenethyl- (6CI, 8CI)  
OTHER NAMES:  
CN (Phenylethyl)biguanide  
CN .beta.-PEBG  
CN .beta.-Phenethylbiguanide

CN 1-Phenethylbiguanide  
CN Cronoformin  
CN DB Comb.  
CN DB-retard  
CN DBI  
CN Debeone  
CN Diabis  
CN Dibiraf  
CN Dibotin  
CN Fenfoduron  
CN Fenformin  
CN Fenormin  
CN Glukopostin  
CN Glyphen  
CN PEDG  
CN Phenethylbiguanide  
CN **Phenformin**  
CN Phenformine  
CN Phenformix  
CN Retardo  
CN W 32

=> d rn cn 15

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 692-13-7 REGISTRY  
CN Imidodicarbonimidic diamide, N-butyl- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Biguanide, 1-butyl- (6CI, 8CI)  
OTHER NAMES:  
CN 1-Butylbiguanide  
CN **Buformin**  
CN Buformine  
CN Butformin  
CN Butylbiguanide  
CN Butyldiguanide  
CN DBV  
CN Glybigid  
CN H 224  
CN N1-Butylbiguanide  
CN W 37

=> d rn cn 16

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 56-03-1 REGISTRY  
CN Imidodicarbonimidic diamide (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN **Biguanide (6CI, 8CI)**  
OTHER NAMES:  
CN Diguanide  
CN Guanidine, (aminoiminomethyl)-  
CN Guanylguanidine  
CN Isobiguanide

=> d rn cn 17

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN

RN 427-51-0 REGISTRY  
CN 3'H-Cyclopropa[1,2]pregna-1,4,6-triene-3,20-dione, 17-(acetyloxy)-6-chloro-1,2-dihydro-, (1.beta.,2.beta.)- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 3'H-Cyclopropa[1,2]pregna-1,4,6-triene-3,20-dione, 6-chloro-1.beta.,2.beta.-dihydro-17-hydroxy-, acetate (8CI)  
CN Cyclopropa[1,2]cyclopenta[a]phenanthrene, 3'H-cyclopropa[1,2]pregna-1,4,6-triene-3,20-dione deriv.  
CN Pregna-4,6-diene-3,20-dione, 6-chloro-17-hydroxy-1.alpha.,2.alpha.-methylene-, acetate (7CI)  
OTHER NAMES:  
CN 1,2.alpha.-Methylene-6-chloro-.DELTA.4,6-pregnadien-17.alpha.-ol-3,20-dione acetate  
CN 1,2.alpha.-Methylene-6-chloro-17.alpha.-acetox-4,6-pregnadiene-3,20-dione  
CN 1,2.alpha.-Methylene-6-chloro-pregna-4,6-diene-3,20-dione 17.alpha.-acetate  
CN 17.alpha.-Acetox-6-chloro-1.alpha.,2.alpha.-methylenepregna-4,6-diene-3,20-dione  
CN 3'H-Cyclopropa[1,2]pregna-1,4,6-triene-3,20-dione  
CN 6-Chloro-1,2.alpha.-methylene-17.alpha.-hydroxy-.DELTA.6-progesterone acetate  
CN 6-Chloro-1,2.alpha.-methylene-6-dehydro-17.alpha.-hydroxyprogesterone acetate  
CN 6-Chloro-17-hydroxy-1.alpha.,2.alpha.-methylenepregna-4,6-diene-3,20-dione acetate  
CN Androcur  
CN CPA  
CN Cyprostat  
CN Cyproterone 17-O-acetate  
CN Cyproterone 17.alpha.-acetate  
CN Cyproterone acetate  
CN Cyproviron  
CN NSC 81430  
CN SH 714

=> d rn cn 18

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 56-03-1 REGISTRY  
CN Imidodicarbonimidic diamide (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Biguanide (6CI, 8CI)  
OTHER NAMES:  
CN Diguanide  
CN Guanidine, (aminoiminomethyl)-  
CN Guanylguanidine  
CN Isobiguanide

=> d rn cn 19

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 13311-84-7 REGISTRY  
CN Propanamide, 2-methyl-N-[4-nitro-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN m-Propionotoluidide, .alpha.,.alpha.,.alpha.-trifluoro-2-methyl-4'-nitro- (8CI)  
OTHER NAMES:  
CN 4'-Nitro-3'-trifluoromethylisobutyranilide

CN 4-Nitro-3-(trifluoromethyl)isobutyranilide  
CN Euflex  
CN Eulexin  
CN Flucinom  
CN Flutamide  
CN N-(Isopropylcarbonyl)-4-nitro-3-trifluoromethylaniline  
CN Niftholide  
CN Niftolide  
CN NSC 147834  
CN NSC 215876  
CN Sch 13521

=> d rn cn l10

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 90357-06-5 REGISTRY  
CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-, (.+-.)-  
OTHER NAMES:  
CN (.+-.)-4'-Cyano-.alpha.,.alpha.,.alpha.-trifluoro-3-[(p-fluorophenyl)sulfonyl]-2-methyl-m-lactotoluidide  
CN Bicalutamide  
CN Casodex  
CN Cosudex  
CN ICI 176334

=> d rn cn l11

L11 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 63612-50-0 REGISTRY  
CN 2,4-Imidazolidinedione, 5,5-dimethyl-3-[4-nitro-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN 1-(3-Trifluoromethyl-4-nitrophenyl)-4,4-dimethylimidazoline-2,5-dione  
CN Anandron  
CN Nilandron  
CN Nilandrone  
CN Nilutamide  
CN RU 23908  
CN RU 23908-10

=> d rn cn l12

L12 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 154992-24-2 REGISTRY  
CN Benzonitrile, 4-[3-(4-hydroxybutyl)-4,4-dimethyl-2,5-dioxo-1-imidazolidinyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN 4-(4,4-Dimethyl-2,5-dioxo-3-(4-hydroxybutyl)1-imidazolidinyl)-2-(trifluoromethyl)benzonitrile  
CN RU 58841

=> d rn cn l113

L113 NOT FOUND

The L-number entered has not been defined in this session, or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> d rn cn 113

L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 976-71-6 REGISTRY  
CN Pregna-4,6-diene-21-carboxylic acid, 17-hydroxy-3-oxo-, .gamma.-lactone,  
(17.alpha.)- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 17.alpha.-Pregna-4,6-diene-21-carboxylic acid, 17-hydroxy-3-oxo-,  
.gamma.-lactone (6CI, 7CI, 8CI)  
CN Spiro[17H-cyclopenta[a]phenanthrene-17,2'(5'H)-furan],  
pregna-4,6-diene-21-carboxylic acid deriv.  
OTHER NAMES:  
CN 11614 R.P.  
CN 17-Hydroxy-3-oxo-17.alpha.-pregna-4,6-diene-21-carboxylic acid  
.gamma.-lactone  
CN 17-Hydroxy-3-oxo-17.alpha.-pregna-4,6-diene-21-carboxylic acid lactone  
CN 17.alpha.-(2-Carboxyethyl)-17.beta.-hydroxyandrosta-4,6-dien-3-one lactone  
CN 17.beta.-Hydroxy-3-oxopregna-4,6-diene-21-carboxylic acid  
CN 20-Spiroxa-4,6-diene-3,21-dione  
CN 3'-(3-Oxo-17.beta.-hydroxyandrosta-4,6-dien-17.alpha.-yl)-propionic acid  
lactone  
CN 3-(17.beta.-Hydroxy-3-oxoandrosta-4,6-dien-17.alpha.-yl)propionic acid  
.gamma.-lactone  
CN 3-(17.beta.-Hydroxy-3-oxoandrosta-4,6-dien-17.alpha.-yl)propionic acid  
lactone  
CN 3-(3-Oxo-17.beta.-hydroxy-4,6-androstadien-17.alpha.-yl)propionic acid  
.gamma.-lactone  
CN Aldadiene  
CN Canrenone  
CN Phanurane  
CN SC 9376  
CN Spirolactone SC 14266

=> d rn cn 114

L14 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 52-01-7 REGISTRY  
CN Pregn-4-ene-21-carboxylic acid, 7-(acetylthio)-17-hydroxy-3-oxo-,  
.gamma.-lactone, (7.alpha.;17.alpha.)- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 17.alpha.-Pregn-4-ene-21-carboxylic acid, 17-hydroxy-7.alpha.-mercapto-3-  
oxo-, .gamma.-lactone, acetate (6CI, 8CI)  
CN Spiro[17H-cyclopenta[a]phenanthrene-17,2'(5'H)-furan],  
pregn-4-ene-21-carboxylic acid deriv.  
OTHER NAMES:  
CN 17-Hydroxy-7.alpha.-mercapto-3-oxo-17.alpha.-pregn-4-ene-21-carboxylic  
acid .gamma.-lactone 7-acetate  
CN 3'-(3-Oxo-7.alpha.-acetylthio-17.beta.-hydroxyandrost-4-en-17.alpha.-yl)-  
propionic acid lactone  
CN 3-(3-keto-7.alpha.-Acetylthio-17.beta.-hydroxy-4-androsten-17.alpha.-  
yl)propionic acid lactone  
CN 3-(3-Oxo-7.alpha.-acetylthio-17.beta.-hydroxy-4-androsten-17.alpha.-  
yl)propionic acid .gamma.-lactone  
CN 7.alpha.-(Acetylthio)-17-hydroxy-3-oxo-17.alpha.-pregn-4-ene-21-carboxylic  
acid .gamma.-lactone  
CN 7.alpha.-Acetylthio-3-oxo-17.alpha.-pregn-4-ene-21,17.beta.-carbolactone

CN Abbolactone  
CN Aldace  
CN Aldactone  
CN Aldactone A  
CN Aldopur  
CN Almatol  
CN Altex  
CN Aquareduct  
CN Deverol  
CN Diatensec  
CN Dira  
CN Duraspiron  
CN Euteberol  
CN Lacalmin  
CN Lacdene  
CN Laractone  
CN Nefurofan  
CN NSC 150399  
CN Osiren  
CN Osyrol  
CN Sagisal  
CN SC 9420  
CN Sincomen  
CN Spiresis  
CN Spiretic  
CN Spiridon  
CN Spiro-Tablinen  
CN Spiroctan  
CN Spiroderm  
CN Spirolactone  
CN Spirolang  
CN Spirolone  
CN Spirone  
CN Spironolactone  
CN Spironolactone A  
CN Supra-Puren  
CN Suracton  
CN Uractone  
CN Urusonin  
CN Verospiron  
CN Verospirone  
CN Xenalon

=> d rn cn l15

L15 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 57-83-0 REGISTRY  
CN Pregn-4-ene-3,20-dione (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN .DELTA.4-Pregnene-3,20-dione  
CN Agolutin  
CN Bio-luton  
CN Corlutin  
CN Corlutina  
CN Corluvite  
CN Corporin  
CN Corpus luteum hormone  
CN Crinone  
CN Cyclogest  
CN Flavolutan

CN Fologenon  
CN Gesterol  
CN Gestiron  
CN Gestone  
CN Gestormone  
CN Gestron  
CN Glanducorpin  
CN Gynlutin  
CN Gynolutone  
CN Hormoflaveine  
CN Hormoluton  
CN Lipo-Lutin  
CN Lucorteam Sol  
CN Lugesteron  
CN Luteal Hormone  
CN Luteinique  
CN Luteocrin normale  
CN Luteodyn  
CN Luteogan  
CN Luteohormone  
CN Luteol  
CN Luteopur  
CN Luteosan  
CN Luteostab  
CN Luteovis  
CN Luteum  
CN Lutex  
CN Lutidon  
CN Lutin  
CN Lutociclina  
CN Lutocucclin M  
CN Lutocyclin  
CN Lutocyclin M  
CN Lutocylin  
CN Lutoform  
CN Lutogyl  
CN Lutren  
CN Lutromone  
CN Nalutron

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for  
DISPLAY

=> d rn cn l16

L16 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN

RN **73671-86-0** REGISTRY

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N,N-diethylhexadecahydro-1,4a,6a-trimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 4-Azaandrostane-17-carboxamide, N,N-diethyl-4-methyl-3-oxo-,  
(5.alpha.,17.beta.)-

OTHER NAMES:

CN 17.beta.-N,N-Diethylcarbamoyl-4-methyl-4-aza-5.alpha.-androstan-3-one

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N,N-diethylhexadecahydro-1,4a,6a-trimethyl-2-oxo-, [4aR-(4a.alpha.,4b.beta.,6a.alpha.,7.alpha.,9a.beta.,9b.alpha.,11a.beta.)]-

CN 4-MA

CN DMAA

=> d rn cn 117

L17 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 65277-42-1 REGISTRY  
CN Piperazine, 1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-, rel- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Piperazine, 1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-, cis-

OTHER NAMES:

CN (.+-.)-Ketoconazole  
CN 34: PN: US20030109453 SEQID: 33 claimed sequence  
CN Fungarest  
CN Fungoral  
CN Ketoconazole  
CN Ketoderm  
CN Ketoisdin  
CN Nizoral  
CN Nizral  
CN Orifungal M  
CN Panfungol  
CN R 41400

=> d rn cn 118

L18 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 51481-61-9 REGISTRY  
CN Guanidine, N-cyano-N'-methyl-N''-[2-[[5-methyl-1H-imidazol-4-yl)methyl]thio]ethyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Acibilin  
CN Acinil  
CN Biomet  
CN Çimal  
CN Cimetag  
CN Cimetidine  
CN Cimetum  
CN Dyspamet  
CN Edalene  
CN Eureceptor  
CN Gastromet  
CN Histodil  
CN N-Cyano-N'-methyl-N''-[2-((4-methyl-5-imidazolyl)-methylthio)ethyl]guanidine  
CN NSC 335308  
CN Peptol  
CN SKF 92334  
CN Tagamet  
CN Tametin  
CN Tratul  
CN Ulcedin  
CN Ulcedine  
CN Ulcerfen  
CN Ulcimet  
CN Ulcofalk  
CN Ulcomedina  
CN Ulcomet  
CN Ulhys

=> file reg; d his 126-128

FILE 'REGISTRY' ENTERED AT 15:03:04 ON 12 AUG 2003

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STRUCTURE FILE UPDATES: 11 AUG 2003 HIGHEST RN 565156-77-6

DICTIONARY FILE UPDATES: 11 AUG 2003 HIGHEST RN 565156-77-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

(FILE 'ZCA' ENTERED AT 14:57:05 ON 12 AUG 2003)

FILE 'CAPLUS' ENTERED AT 14:59:00 ON 12 AUG 2003  
S L3/CRN OR METFORMIN OR NNDG

FILE 'REGISTRY' ENTERED AT 14:59:22 ON 12 AUG 2003

FILE 'CAPLUS' ENTERED AT 14:59:22 ON 12 AUG 2003

FILE 'REGISTRY' ENTERED AT 14:59:54 ON 12 AUG 2003

L26	130 S 657-24-9/CRN	<i>metformin</i>
L27	55 S 114-86-3/CRN	<i>phenformin</i>
L28	24 S 692-13-7/CRN	<i>buformin</i>

FILE 'REGISTRY' ENTERED AT 15:03:04 ON 12 AUG 2003

=> d his 132

(FILE 'REGISTRY' ENTERED AT 15:04:26 ON 12 AUG 2003)

L32 65 S 56-03-1/CRN *biguanide*

=> file caplus; d que 145; d que 149; d que 152; d que 153; d que 155

FILE 'CAPLUS' ENTERED AT 16:42:35 ON 12 AUG 2003

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FILE COVERS 1907 - 12 Aug 2003 VOL 139 ISS 7  
FILE LAST UPDATED: 11 Aug 2003 (20030811/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L19	2087	SEA FILE=CAPLUS ABB=ON PLU=ON	ALOPECIA/CT
L20	2584	SEA FILE=CAPLUS ABB=ON PLU=ON	BALD?
L21	1680	SEA FILE=CAPLUS ABB=ON PLU=ON	HAIR (2A) LOSS
L26	130	SEA FILE=REGISTRY ABB=ON PLU=ON	657-24-9/CRN
L27	55	SEA FILE=REGISTRY ABB=ON PLU=ON	114-86-3/CRN
L28	24	SEA FILE=REGISTRY ABB=ON PLU=ON	692-13-7/CRN
L29	1607	SEA FILE=CAPLUS ABB=ON PLU=ON	L26 OR METFORMIN OR NNDG
L30	832	SEA FILE=CAPLUS ABB=ON PLU=ON	L27 OR PHENFORMIN OR W 32
L31	516	SEA FILE=CAPLUS ABB=ON PLU=ON	L28 OR BUFORMIN OR H 224 OR W 34 OR DBV
L32	65	SEA FILE=REGISTRY ABB=ON PLU=ON	56-03-1/CRN
L33	4790	SEA FILE=CAPLUS ABB=ON PLU=ON	L32 OR ?BIGUANIDE
L45	2	SEA FILE=CAPLUS ABB=ON PLU=ON	(L19 OR L20 OR L21) AND ((L29 OR L30 OR L31) OR L33)
L7	1	SEA FILE=REGISTRY ABB=ON PLU=ON	427-51-0/RN
L9	1	SEA FILE=REGISTRY ABB=ON PLU=ON	13311-84-7/RN
L10	1	SEA FILE=REGISTRY ABB=ON PLU=ON	90357-06-5/RN
L11	1	SEA FILE=REGISTRY ABB=ON PLU=ON	63612-50-0/RN
L12	1	SEA FILE=REGISTRY ABB=ON PLU=ON	154992-24-2/RN
L13	1	SEA FILE=REGISTRY ABB=ON PLU=ON	976-71-6/RN
L14	1	SEA FILE=REGISTRY ABB=ON PLU=ON	52-01-7/RN
L15	1	SEA FILE=REGISTRY ABB=ON PLU=ON	57-83-0/RN
L16	1	SEA FILE=REGISTRY ABB=ON PLU=ON	73671-86-0/RN
L17	1	SEA FILE=REGISTRY ABB=ON PLU=ON	65277-42-1/RN
L18	1	SEA FILE=REGISTRY ABB=ON PLU=ON	51481-61-9/RN
L19	2087	SEA FILE=CAPLUS ABB=ON PLU=ON	ALOPECIA/CT
L20	2584	SEA FILE=CAPLUS ABB=ON PLU=ON	BALD?
L21	1680	SEA FILE=CAPLUS ABB=ON PLU=ON	HAIR (2A) LOSS
L34	1945	SEA FILE=CAPLUS ABB=ON PLU=ON	L7 OR CYPROTERONE ACETATE OR NSC 81430 OR SH 714
L35	1330	SEA FILE=CAPLUS ABB=ON PLU=ON	L9 OR FLUTAMIDE OR NSC (W) (147834 04 215876) OR SCH 13521
L36	340	SEA FILE=CAPLUS ABB=ON PLU=ON	L10 OR BICALUTAMIDE OR ICI 176334
L37	164	SEA FILE=CAPLUS ABB=ON PLU=ON	L11 OR NILUTAMIDE OR RU 23908?
L38	24	SEA FILE=CAPLUS ABB=ON PLU=ON	L12 OR RU58841
L39	364	SEA FILE=CAPLUS ABB=ON PLU=ON	L13 OR CANRERONE OR SC 9376 OR SPIROLACTONE SC 14266
L40	2708	SEA FILE=CAPLUS ABB=ON PLU=ON	L14 OR SPIRONOLACTONE OR NSC 150399
L41	59664	SEA FILE=CAPLUS ABB=ON PLU=ON	L15 OR PROGESTERONE
L42	2384	SEA FILE=CAPLUS ABB=ON PLU=ON	L16 OR 4 MA OR DMAA
L43	3385	SEA FILE=CAPLUS ABB=ON PLU=ON	L17 OR KETOCONAZOLE

L44 7677 SEA FILE=CAPLUS ABB=ON PLU=ON L18 OR CIMETIDINE OR SKF 92334  
 OR NSC 335308  
 L47 36 SEA FILE=CAPLUS ABB=ON PLU=ON DRUG DELIVERY SYSTEMS/CT (L)  
 (ALOPECIA)  
 L49 2 SEA FILE=CAPLUS ABB=ON PLU=ON (L19 OR L20 OR L21) AND (L34  
 OR L35 OR L36 OR L37 OR L38 OR L39 OR L40 OR L41 OR L42 OR L43  
 OR L44) AND L47  
  
 L26 130 SEA FILE=REGISTRY ABB=ON PLU=ON 657-24-9/CRN  
 L27 55 SEA FILE=REGISTRY ABB=ON PLU=ON 114-86-3/CRN  
 L28 24 SEA FILE=REGISTRY ABB=ON PLU=ON 692-13-7/CRN  
 L29 1607 SEA FILE=CAPLUS ABB=ON PLU=ON L26 OR METFORMIN OR NNDG  
 L30 832 SEA FILE=CAPLUS ABB=ON PLU=ON L27 OR PHENFORMIN OR W 32  
 L31 516 SEA FILE=CAPLUS ABB=ON PLU=ON L28 OR BUFORMIN OR H 224 OR W  
 34 OR DBV  
 L32 65 SEA FILE=REGISTRY ABB=ON PLU=ON 56-03-1/CRN  
 L33 4790 SEA FILE=CAPLUS ABB=ON PLU=ON L32 OR ?BIGUANIDE  
 L47 36 SEA FILE=CAPLUS ABB=ON PLU=ON DRUG DELIVERY SYSTEMS/CT (L)  
 (ALOPECIA)  
 L52 1 SEA FILE=CAPLUS ABB=ON PLU=ON ((L29 OR L30 OR L31) OR L33)  
 AND L47  
  
 L25 1693 SEA FILE=CAPLUS ABB=ON PLU=ON HAIR PREPARATIONS/CT (L)  
 GROWTH  
 L26 130 SEA FILE=REGISTRY ABB=ON PLU=ON 657-24-9/CRN  
 L27 55 SEA FILE=REGISTRY ABB=ON PLU=ON 114-86-3/CRN  
 L28 24 SEA FILE=REGISTRY ABB=ON PLU=ON 692-13-7/CRN  
 L29 1607 SEA FILE=CAPLUS ABB=ON PLU=ON L26 OR METFORMIN OR NNDG  
 L30 832 SEA FILE=CAPLUS ABB=ON PLU=ON L27 OR PHENFORMIN OR W 32  
 L31 516 SEA FILE=CAPLUS ABB=ON PLU=ON L28 OR BUFORMIN OR H 224 OR W  
 34 OR DBV  
 L32 65 SEA FILE=REGISTRY ABB=ON PLU=ON 56-03-1/CRN  
 L33 4790 SEA FILE=CAPLUS ABB=ON PLU=ON L32 OR ?BIGUANIDE  
 L53 4 SEA FILE=CAPLUS ABB=ON PLU=ON ((L29 OR L30 OR L31) OR L33)  
 AND L25  
  
 L7 1 SEA FILE=REGISTRY ABB=ON PLU=ON 427-51-0/RN  
 L9 1 SEA FILE=REGISTRY ABB=ON PLU=ON 13311-84-7/RN  
 L10 1 SEA FILE=REGISTRY ABB=ON PLU=ON 90357-06-5/RN  
 L11 1 SEA FILE=REGISTRY ABB=ON PLU=ON 63612-50-0/RN  
 L12 1 SEA FILE=REGISTRY ABB=ON PLU=ON 154992-24-2/RN  
 L13 1 SEA FILE=REGISTRY ABB=ON PLU=ON 976-71-6/RN  
 L14 1 SEA FILE=REGISTRY ABB=ON PLU=ON 52-01-7/RN  
 L15 1 SEA FILE=REGISTRY ABB=ON PLU=ON 57-83-0/RN  
 L16 1 SEA FILE=REGISTRY ABB=ON PLU=ON 73671-86-0/RN  
 L17 1 SEA FILE=REGISTRY ABB=ON PLU=ON 65277-42-1/RN  
 L18 1 SEA FILE=REGISTRY ABB=ON PLU=ON 51481-61-9/RN  
 L20 2584 SEA FILE=CAPLUS ABB=ON PLU=ON BALD?  
 L21 1680 SEA FILE=CAPLUS ABB=ON PLU=ON HAIR (2A) LOSS  
 L26 130 SEA FILE=REGISTRY ABB=ON PLU=ON 657-24-9/CRN  
 L27 55 SEA FILE=REGISTRY ABB=ON PLU=ON 114-86-3/CRN  
 L28 24 SEA FILE=REGISTRY ABB=ON PLU=ON 692-13-7/CRN  
 L29 1607 SEA FILE=CAPLUS ABB=ON PLU=ON L26 OR METFORMIN OR NNDG  
 L30 832 SEA FILE=CAPLUS ABB=ON PLU=ON L27 OR PHENFORMIN OR W 32  
 L31 516 SEA FILE=CAPLUS ABB=ON PLU=ON L28 OR BUFORMIN OR H 224 OR W

34 OR DBV  
L32 65 SEA FILE=REGISTRY ABB=ON PLU=ON 56-03-1/CRN  
L33 4790 SEA FILE=CAPLUS ABB=ON PLU=ON L32 OR ?BIGUANIDE  
L34 1945 SEA FILE=CAPLUS ABB=ON PLU=ON L7 OR CYPROTERONE ACETATE OR  
NSC 81430 OR SH 714  
L35 1330 SEA FILE=CAPLUS ABB=ON PLU=ON L9 OR FLUTAMIDE OR NSC (W)  
(147834 04 215876) OR SCH 13521  
L36 340 SEA FILE=CAPLUS ABB=ON PLU=ON L10 OR BICALUTAMIDE OR ICI  
176334  
L37 164 SEA FILE=CAPLUS ABB=ON PLU=ON L11 OR NILUTAMIDE OR RU 23908?  
L38 24 SEA FILE=CAPLUS ABB=ON PLU=ON L12 OR RU58841  
L39 364 SEA FILE=CAPLUS ABB=ON PLU=ON L13 OR CANRERONE OR SC 9376 OR  
SPIROLACTONE SC 14266  
L40 2708 SEA FILE=CAPLUS ABB=ON PLU=ON L14 OR SPIRONOLACTONE OR NSC  
150399  
L41 59664 SEA FILE=CAPLUS ABB=ON PLU=ON L15 OR PROGESTERONE  
L42 2384 SEA FILE=CAPLUS ABB=ON PLU=ON L16 OR 4 MA OR DMAA  
L43 3385 SEA FILE=CAPLUS ABB=ON PLU=ON L17 OR KETOCONAZOLE  
L44 7677 SEA FILE=CAPLUS ABB=ON PLU=ON L18 OR CIMETIDINE OR SKF 92334  
OR NSC 335308  
L55 2 SEA FILE=CAPLUS ABB=ON PLU=ON ((L29 OR L30 OR L31) OR L33)  
AND (L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR L40 OR L41 OR  
L42 OR L43 OR L44) AND (?ALOPECIA? OR (L20 OR L21))

=> s l45 or l49 or l52 or l53 or l55

L95 6 L45 OR L49 OR L52 OR L53 OR L55

=> file medline; d que l63

FILE 'MEDLINE' ENTERED AT 16:43:05 ON 12 AUG 2003

FILE LAST UPDATED: 9 AUG 2003 (20030809/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the  
MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html>  
for a description on changes.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

L58 8358 SEA FILE=MEDLINE ABB=ON PLU=ON BIGUANIDES+NT/CT  
L59 158 SEA FILE=MEDLINE ABB=ON PLU=ON PHENYL BIGUANIDE/CN  
L61 6415 SEA FILE=MEDLINE ABB=ON PLU=ON ALOPECIA+NT/CT  
L62 14339 SEA FILE=MEDLINE ABB=ON PLU=ON HAIR/CT OR HAIR FOLLICLE/CT  
L63 8 SEA FILE=MEDLINE ABB=ON PLU=ON (L58 OR L59) AND (L61 OR L62)

=> file embase; d que l75

FILE 'EMBASE' ENTERED AT 16:43:14 ON 12 AUG 2003

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FILE COVERS 1974 TO 10 Aug 2003 (20030810/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate

substance identification.

L71 9771 SEA FILE=EMBASE ABB=ON PLU=ON BIGUANIDE/CT OR BIGUANIDE  
DERIVATIVE+NT/CT  
L72 88066 SEA FILE=EMBASE ABB=ON PLU=ON CYPROTERONE ACETATE/CT OR  
FLUTAMIDE/CT OR BICALUTAMIDE/CT OR NILUTAMIDE/CT OR RU  
58841/CT OR CANRENONE/CT OR SPIRONOLACTONE/CT OR PROGESTERONE+N  
T/CT OR 4 MA OR KETOCONAZOLE/CT OR CIMETIDINE/CT  
L73 45190 SEA FILE=EMBASE ABB=ON PLU=ON ALOPECIA OR HAIR (2A) LOSS OR  
HAIR OR HAIRLE? OR BALD?  
L75 17 SEA FILE=EMBASE ABB=ON PLU=ON L71 AND L72 AND L73

=> file biosis; d que 180

FILE 'BIOSIS' ENTERED AT 16:43:22 ON 12 AUG 2003  
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FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 6 August 2003 (20030806/ED)

L76 4041 SEA FILE=BIOSIS ABB=ON PLU=ON METFORMIN? OR PHENFORMIN? OR  
BUFORMIN? OR ?BIGUANIDE?  
L77 88955 SEA FILE=BIOSIS ABB=ON PLU=ON CYPROTERONE ACETATE OR  
FLUTAMIDE OR BICALUTAMIDE OR NILUTAMIDE OR RU 58841 OR  
CANRENONE OR SPIRONOLACTONE OR PROGESTERONE OR 4 MA OR  
KETOCONAZOLE OR CIMETIDINE  
L78 77217 SEA FILE=BIOSIS ABB=ON PLU=ON ALOPECIA OR HIRSUT? OR HAIR?  
OR BALD?  
L80 7 SEA FILE=BIOSIS ABB=ON PLU=ON L76 AND L77 AND L78

=> file wpid; d que 189; d que 191

FILE 'WPIDS' ENTERED AT 16:43:34 ON 12 AUG 2003  
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FILE LAST UPDATED: 8 AUG 2003 <20030808/UP>  
MOST RECENT DERWENT UPDATE: 200351 <200351/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,  
SEE <http://www.derwent.com/dwpi/updates/dwpicov/index.html> <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
PLEASE VISIT:  
[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER  
GUIDES, PLEASE VISIT:  
[http://www.derwent.com/userguides/dwpi\\_guide.html](http://www.derwent.com/userguides/dwpi_guide.html) <<<

L81 1202 SEA FILE=WPIDS ABB=ON PLU=ON METFORMIN? OR PHENFORMIN? OR  
 BUFORMIN? OR ?BIGUANIDE?  
 L82 208 SEA FILE=WPIDS ABB=ON PLU=ON CYPROTERONE ACETATE OR NSC (W)  
 (81340 OR 81430) OR SH 714 OR FLUTAMIDE OR NSC (W) (147834 OR  
 215876) OR SCH 13521  
 L88 4 SEA FILE=WPIDS ABB=ON PLU=ON L81 AND L82  
 L89 1 SEA FILE=WPIDS ABB=ON PLU=ON L88 AND OVARY/TI

L81 1202 SEA FILE=WPIDS ABB=ON PLU=ON METFORMIN? OR PHENFORMIN? OR  
 BUFORMIN? OR ?BIGUANIDE?  
 L85 47841 SEA FILE=WPIDS ABB=ON PLU=ON ALOPECIA OR HIRSUT? OR HAIR?  
 OR BALD?  
 L86 22 SEA FILE=WPIDS ABB=ON PLU=ON L81 AND L85  
 L90 11 SEA FILE=WPIDS ABB=ON PLU=ON L86 AND A61K?/ICM,ICS  
 L91 3 SEA FILE=WPIDS ABB=ON PLU=ON L90 AND (ANTIDIABET? OR CAPILL?  
 OR SURGICAL)/TI

=> s 189 or 191

L96 4 L89 OR L91

=> dup rem 163 195 175 180 196

FILE 'MEDLINE' ENTERED AT 16:44:14 ON 12 AUG 2003

FILE 'CAPLUS' ENTERED AT 16:44:14 ON 12 AUG 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE 'BIOSIS' ENTERED AT 16:44:14 ON 12 AUG 2003

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FILE 'WPIDS' ENTERED AT 16:44:14 ON 12 AUG 2003

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PROCESSING COMPLETED FOR L63

PROCESSING COMPLETED FOR L95

PROCESSING COMPLETED FOR L75

PROCESSING COMPLETED FOR L80

PROCESSING COMPLETED FOR L96

L97 40 DUP REM L63 L95 L75 L80 L96 (2 DUPLICATES REMOVED)

ANSWERS '1-8' FROM FILE MEDLINE

ANSWERS '9-13' FROM FILE CAPLUS

ANSWERS '14-30' FROM FILE EMBASE

ANSWERS '31-37' FROM FILE BIOSIS

ANSWERS '38-40' FROM FILE WPIDS

=> d ibib ab 197 1-40

L97 ANSWER 1 OF 40

MEDLINE on STN

DUPLICATE 1

ACCESSION NUMBER: 2002404418 MEDLINE

DOCUMENT NUMBER: 22148685 PubMed ID: 12153743

TITLE: The effect of metformin on hirsutism in polycystic ovary syndrome.

AUTHOR: Kelly Christopher J G; Gordon Derek

CORPORATE SOURCE: Stobhill Hospital, North Glasgow University NHS Trust,  
 Glasgow, G21 3UW, UK.. c.kelly@clinmed.gla.ac.uk

SOURCE: EUROPEAN JOURNAL OF ENDOCRINOLOGY, (2002 Aug) 147 (2)  
217-21.  
Journal code: 9423848. ISSN: 0804-4643.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(RANDOMIZED CONTROLLED TRIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200209  
ENTRY DATE: Entered STN: 20020803  
Last Updated on STN: 20020925  
Entered Medline: 20020924

AB OBJECTIVE: Polycystic ovary syndrome (PCOS) is a common reproductive disorder characterised by insulin resistance and often associated with hirsutism. Insulin sensitising agents, such as metformin, improve both the biochemical and reproductive parameters; however, no study has been designed to specifically assess the effect of metformin on hair growth. DESIGN AND PATIENTS: Sixteen women with PCOS and hirsutism were enrolled into a 14 month (two 6 month phases with a 2 month washout) double-blind placebo-controlled cross over study. MEASUREMENTS: Hirsutism was assessed using the Ferriman and Gallwey (F-G) score, patient self-assessment and growth velocity. Weight, height and waist-hip ratio were recorded. Gonadotrophins, androgens, plasma glucose and lipids were also measured. RESULTS: Ten women completed the full 14 month study. There was a significant improvement in hirsutism at the end of the metformin phase compared with placebo: F-G score  $15.8 \pm 1.4$  vs  $17.5 \pm 1.2$  ( $P=0.025$ ) and patient self-assessment  $2.4 \pm 0.1$  vs  $3.3 \pm 0.3$  ( $P=0.014$ ). Growth velocity, in millimetres per day at the end of each phase also improved ( $0.67 \pm 0.17$  vs  $0.77 \pm 0.11$ ;  $P=0.03$ ). There was a non-significant improvement in both sex hormone binding globulin (SHBG) and free androgen index (FAI), although there was a significant difference between baseline and metformin treatment for SHBG ( $P=0.023$ ) and FAI ( $P=0.036$ ). Metformin treatment also reduced weight significantly ( $91.5 \pm 7.6$  vs  $94.0 \pm 9.8$  kg;  $P=0.009$ ) and led to a significant improvement in cycle frequency ( $0.53 \pm 0.12$  vs  $0.35 \pm 0.08$  cycles per month;  $P=0.008$ ). CONCLUSION: We have demonstrated that metformin treatment in a group of women with PCOS results in a clinically and statistically significant improvement in hair growth compared with placebo.

L97 ANSWER 2 OF 40 MEDLINE on STN  
ACCESSION NUMBER: 2003324975 MEDLINE  
DOCUMENT NUMBER: 22738586 PubMed ID: 12854769  
TITLE: Implantation of deep brain stimulation electrodes in  
unshaved patients.  
COMMENT: Comment on: J Neurosurg. 2002 Dec;97(6):1476-8  
AUTHOR: Plaha Puneet; Patel Nikunj K; Gill Steven S  
SOURCE: JOURNAL OF NEUROSURGERY, (2003 Jul) 99 (1) 207-8; author  
reply 208-9.  
Journal code: 0253357. ISSN: 0022-3085.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Commentary  
Letter  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 200308  
ENTRY DATE: Entered STN: 20030713  
Last Updated on STN: 20030809  
Entered Medline: 20030808

L97 ANSWER 3 OF 40 MEDLINE on STN

ACCESSION NUMBER: 2000266880 MEDLINE  
DOCUMENT NUMBER: 20266880 PubMed ID: 10806917  
TITLE: [Trichological examinations in women suffering from diabetes mellitus].  
Badania trichologiczne u kobiet chorych na cukrzyce.  
AUTHOR: Brzezinska-Wcislo L; Bogdanowski T; Koslacz E; Hawrot A  
CORPORATE SOURCE: I Katedry i Kliniki Dermatologii Slaskiej Akademii Medycznej w Katowicach.  
SOURCE: WIADOMOSCI LEKARSKIE, (2000) 53 (1-2) 30-4.  
Journal code: 9705467. ISSN: 0043-5147.  
PUB. COUNTRY: Poland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: Polish  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200007  
ENTRY DATE: Entered STN: 20000720  
Last Updated on STN: 20000720  
Entered Medline: 20000711

AB The lack of data on the process of alopecia in women suffering from diabetes mellitus made us undertake research in this area. The aim of this paper was the assessment of the state of head hair in trichological and clinical examinations, and on the basis of questionnaire. 50 women (age 44-82 years) were included in the study. Alopecia in women with diabetes mellitus is diffuse, located on the apex of the head and basic hair loss lies in telogenic pathomechanism. The highest percentage of telogenic hair is found in women treated with biguanides, and the lowest one in female patients taking insulin.

L97 ANSWER 4 OF 40 MEDLINE on STN  
ACCESSION NUMBER: 95015129 MEDLINE  
DOCUMENT NUMBER: 95015129 PubMed ID: 7929925  
TITLE: Surgical pearl: tips for scalp surgery.  
AUTHOR: Salasche S J  
CORPORATE SOURCE: Section of Dermatology, University of Arizona Health Science Center, Tucson 85724.  
SOURCE: JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY, (1994 Nov) 31 (5 Pt 1) 791-2.  
Journal code: 7907132. ISSN: 0190-9622.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199411  
ENTRY DATE: Entered STN: 19941222  
Last Updated on STN: 19941222  
Entered Medline: 19941117

L97 ANSWER 5 OF 40 MEDLINE on STN  
ACCESSION NUMBER: 89096227 MEDLINE  
DOCUMENT NUMBER: 89096227 PubMed ID: 2563137  
TITLE: Hairloss and scaling with proguanil.  
AUTHOR: Hanson S N; Kuylen K; Bjorkman A B  
SOURCE: LANCET, (1989 Jan 28) 1 (8631) 225.  
Journal code: 2985213R. ISSN: 0140-6736.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Letter  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 198902  
ENTRY DATE: Entered STN: 19900308  
Last Updated on STN: 19970203

Entered Medline: 19890223

L97 ANSWER 6 OF 40 MEDLINE on STN  
ACCESSION NUMBER: 89142830 MEDLINE  
DOCUMENT NUMBER: 89142830 PubMed ID: 2563814  
TITLE: Proguanil.  
AUTHOR: Fleming A F  
SOURCE: LANCET, (1989 Feb 25) 1 (8635) 439.  
Journal code: 2985213R. ISSN: 0140-6736.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Letter  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 198903  
ENTRY DATE: Entered STN: 19900306  
Last Updated on STN: 19970203  
Entered Medline: 19890330

L97 ANSWER 7 OF 40 MEDLINE on STN  
ACCESSION NUMBER: 84034136 MEDLINE  
DOCUMENT NUMBER: 84034136 PubMed ID: 6195235  
TITLE: Total body bathing with 'Hibiscrub' (chlorhexidine) in surgical patients: a controlled trial.  
AUTHOR: Leigh D A; Stronge J L; Marriner J; Sedgwick J  
SOURCE: JOURNAL OF HOSPITAL INFECTION, (1983 Sep) 4 (3) 229-35.  
Journal code: 8007166. ISSN: 0195-6701.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: (CLINICAL TRIAL)  
(CONTROLLED CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198312  
ENTRY DATE: Entered STN: 19900319  
Last Updated on STN: 19980206  
Entered Medline: 19831220

AB Total body bathing with 'Hibiscrub' (chlorhexidine-detergent) solution was compared with non-medicated soap in 224 patients admitted for surgery. Some 9.6 per cent of patients were found to be nasal carriers of Staphylococcus aureus on admission but 17.3 per cent were colonized at some time during their inpatient stay. Skin colonization by Staph. aureus was only seen in four patients (2 per cent), three were cleared by 'Hibiscrub' bathing but carriage persisted in the other patient who used non-medicated soap. A greater reduction in the total bacterial count on the skin and in the perianal region was seen in patients using 'Hibiscrub'. An increase in the bacterial count was frequently seen in patients using non-medicated soap. Postoperative staphylococcal wound infection occurred in nine patients (4-0 per cent) but nasal or skin carriage was only present in two patients. Although there was no difference in the rates of infection using 'Hibiscrub' or ordinary soap, pre-operative bathing with 'Hibiscrub' may be beneficial as there is a greater reduction in the total bacterial count. The use of non-medicated soap is of dubious value and may even increase the numbers of bacteria on the skin.

L97 ANSWER 8 OF 40 MEDLINE on STN  
ACCESSION NUMBER: 73215221 MEDLINE  
DOCUMENT NUMBER: 73215221 PubMed ID: 4515581  
TITLE: Caries control in the albino rat with chlorhexidine gluconate (Hibitane).  
AUTHOR: Kornman K S; Clark W B; Kreitzman S N; Alvarez C

SOURCE: ARCHIVES OF ORAL BIOLOGY, (1973 Feb) 18 (2) 165-70.  
 Journal code: 0116711. ISSN: 0003-9969.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Dental Journals; Priority Journals  
 ENTRY MONTH: 197309  
 ENTRY DATE: Entered STN: 19900310  
 Last Updated on STN: 19970203  
 Entered Medline: 19730912

L97 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2  
 ACCESSION NUMBER: 2001:730517 CAPLUS  
 DOCUMENT NUMBER: 135:277721  
 TITLE: Cosmetic compositions containing antiandrogenic  
 sterols with retarding action on the regrowth of  
 superfluous hair  
 INVENTOR(S): Di Pierro, Francesco  
 PATENT ASSIGNEE(S): Indena S.P.A., Italy  
 SOURCE: PCT Int. Appl., 17 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072266	A1	20011004	WO 2001-EP1522	20010212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1265586	A1	20021218	EP 2001-909738	20010212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002004519	A	20021125	NO 2002-4519	20020920
PRIORITY APPLN. INFO.: IT 2000-MI628 A 20000324 WO 2001-EP1522 W 20010212				
AB The present invention relates to cosmetic compns. having retarding action on the regrowth of superfluous hair, more particularly to cosmetic compns. contg. fatty acids and antiandrogenic sterols from serenoa (Serenoa repens) and/or from Cucurbita seeds (Cucurbita pepo). A hair gel contained Sernoa repens lipophilic ext. 2.00, ruscogenins 0.30, 20% zanthoxylum bungenanum ext. 0.50, ethanol 20.00, Softigen-767 15.00, propylene glycol 10.00, Oleth-20 5.00, dimethicone copolyol 2.50, carbomer 2.00, triethanolamine 1.00, zinc ricinoleate 0.20, menthol 0.50, preservatives q.s., antioxidants q.s., and water q.s. 100.00 g. REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L97 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN  
 ACCESSION NUMBER: 2003:590896 CAPLUS  
 TITLE: Methods and compositions for treating polycystic ovary  
 syndrome and related symptoms using glucagon-like  
 peptide 1

INVENTOR(S): Hathaway, David R.  
 PATENT ASSIGNEE(S): Restoragen, Inc., USA  
 SOURCE: PCT Int. Appl., 21 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061362	A2	20030731	WO 2003-US1109	20030114

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO,  
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,  
 ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
 NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,  
 ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-350395P P 20020122  
 US 2002-317126 A 20021211

AB The present invention relates to methods of treating polycystic ovary syndrome (PCOS) and related symptoms comprising administering glucagon-like peptide-1 (GLP-1) to subjects suffering therefrom. Methods for the co-administration with ovulation-inducing drugs, anti-androgenic drugs, insulin-sensitizing agents and glucose are also claimed.

L97 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:978338 CAPLUS

DOCUMENT NUMBER: 138:44664

TITLE: Cosmetic compositions having retarding action on the regrowth of superfluous hair

INVENTOR(S): Di Pierro, Francesco

PATENT ASSIGNEE(S): Italy

SOURCE: U.S. Pat. Appl. Publ., 6 pp., Cont.-in-part of U.S. Ser. No. 781,301, abandoned.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002197290	A1	20021226	US 2002-152805	20020523
US 2001033849	A1	20011025	US 2001-781301	20010213

PRIORITY APPLN. INFO.: IT 2000-MI628 A 20000324  
 US 2001-781301 B2 20010213

AB The present invention relates to cosmetic compns. having retarding action on the regrowth of superfluous hair, more particularly to cosmetic compns. contg. lipophilic exts. of Serenoa (Serenoa repens) enriched in fatty acids and with a reduced content of sterols. Prepn. of Serenoa ext. and cosmetic prepn. contg. this ext. is disclosed.

L97 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:840448 CAPLUS

DOCUMENT NUMBER: 137:333064

TITLE: Comparative efficacy of various treatment regimens for

androgenetic alopecia in men  
 AUTHOR(S): Khandpur, Sujay; Suman, Mansi; Reddy, Belum Sivanagi  
 CORPORATE SOURCE: Department of Dermatology and S.T.D., Maulana Azad  
 Meical College and Associated Lok Nayak Hospital, New  
 Delhi, India  
 SOURCE: Journal of Dermatology (2002), 29(8), 489-498  
 CODEN: JDMYAG; ISSN: 0385-2407  
 PUBLISHER: Japanese Dermatological Association  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Our understanding of the etiol. of androgenetic alopecia (AGA) has substantially increased in recent years. As a result, several treatment modalities have been tried with promising results esp. in early stages of AGA. However, as far as has been ascertained, there is no comprehensive study comparing the efficacy of these agents alone and in combination with each other. One hundred male patients with AGA of Hamilton grades II to IV were enrolled in an open, randomized, parallel-group study, designed to evaluate and compare the efficacy of oral finasteride (1 mg per day), topical 2% minoxidil soln. and topical 2% **ketoconazole** shampoo alone and in combination. They were randomized into four groups. Group I (30 patients) was administered oral finasteride, Group II (36 patients) was given a combination of finasteride and topical minoxidil, Group III (24 patients) applied minoxidil alone and Group IV (10 patients) was administered finasteride with topical **ketoconazole**. Treatment efficacy was assessed on the basis of patient and physician assessment scores and global photog. review during the study period of one year. At the end of one year, hair growth was obsd. in all the groups with best results recorded with a combination of finasteride and minoxidil (Group II) followed by groups IV, I and III. Subjects receiving finasteride alone or in combination with minoxidil or **ketoconazole** showed statistically significant improvement ( $p < 0.05$ ) over minoxidil only recipients. No significant side-effects related to the drugs were obsd. In conclusion, it is inferred that the therapeutic efficacy is enhanced by combining the two drugs acting on different etiol. aspects of AGA.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L97 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:635880 CAPLUS  
 DOCUMENT NUMBER: 135:200473  
 TITLE: Methods and compositions based on insulin-sensitivity increasing substances for the treatment of **alopecia** and other disorders of the pilosebaceous apparatus  
 INVENTOR(S): Krajcik, Rozlyn A.; Orentreich, Norman  
 PATENT ASSIGNEE(S): Orentreich Foundation for the Advancement of Science, Inc., USA  
 SOURCE: PCT Int. Appl., 22 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062237	A2	20010830	WO 2001-US5653	20010223
WO 2001062237	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,				

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 1267850 A2 20030102 EP 2001-914437 20010223  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 US 2002143039 A1 20021003 US 2002-73607 20020211  
 PRIORITY APPLN. INFO.: US 2000-184398P P 20000223  
 WO 2001-US5653 W 20010223  
 AB Insulin sensitivity increasing substances (ISIS), including but not  
 limited to D-chiro-inositol, thiazolidinedione and derivs., and  
 biguanides, are useful in the treatment of **hair loss**  
 and other disorders of the pilosebaceous app. (hirsutism, acne, etc.)  
 assocd. with conditions of excess insulin and/or insulin resistance. The  
 treatment comprises administering to a mammal, such as a human, at least  
 one ISIS either alone or in combination with at least one agent, such as  
 an androgen receptor blocker (ARB) and/or a steroid enzyme inhibitor or  
 inducer (STI). Addnl., an activity enhancing agent may be included for  
 topical administration. For example, the onset of age-dependent  
**hair loss** in female ob/ob (obese) mice was delayed by  
 oral **metformin**-HCl treatment using a dose of 240 mg/kg. Clear  
 differences were seen between the incidence of **hair loss**  
 in control vs. **metformin** HCl-treated animals in animals that  
 were older than 300 days. The incidence of **hair loss**  
 in **metformin** HCl-treated animals at 370 days of age was 30%  
 compared to 60% incidence of **hair loss** in non-treated  
 animals. In animals that were 300 days of age, about 20% of the  
**metformin** HCl-treated animals exhibited **hair**  
**loss** in contrast to the control animals, which showed about a 40%  
 incidence of **hair loss**. Addnl., it was noted in the  
 study that obese mice were prone to a spontaneous skin condition which may  
 resemble human acanthosis nigricans or migratory ichthyosis. Although  
 this condition was not fully characterized, the **metformin**  
 HCl-treated animal group exhibited markedly less incidence of this skin  
 condition relative to the control animals, the majority of which were  
 affected by the skin condition. In addn., transient changes in  
**hair loss** patterns were occasionally noted in some of  
 the animals during the course of the study. For example, an animal which  
 presented with very moderate **hair loss** (i.e., only  
 possible thinning of hair coat) for a period of 2-3 wk might later exhibit  
 no **hair loss** and sustain that grade for an extended  
 period of time.  
 L97 ANSWER 14 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
 ACCESSION NUMBER: 2003257952 EMBASE  
 TITLE: Evaluation and treatment of women with hirsutism.  
 AUTHOR: Hunter M.H.; Carek P.J.  
 CORPORATE SOURCE: Dr. M.H. Hunter, University Family Medicine, 9298 Medical  
 Plaza Dr., N., Charleston, SC 29406, United States.  
 hunterlh@musc.edu  
 SOURCE: American Family Physician, (15 Jun 2003) 67/12 (2565-2572).  
 Refs: 35  
 ISSN: 0002-838X CODEN: AFPYAE  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 003 Endocrinology  
 013 Dermatology and Venereology  
 037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Hirsutism is a common disorder, often resulting from conditions that are not life-threatening. It may signal more serious clinical pathology, and clinical evaluation should differentiate benign causes from tumors or other conditions such as polycystic ovary syndrome, late-onset adrenal hyperplasia, and Cushing's syndrome. Laboratory testing should be based on the patient's history and physical findings, but screening for levels of serum testosterone and 17.alpha.-hydroxyprogesterone is sufficient in most cases. Women with irregular menses and hirsutism should be screened for thyroid dysfunction and prolactin disorders. Pharmacologic and/or nonpharmacologic treatments may be used. Advances in laser **hair** removal methods and topical **hair** growth retardants offer new options. The use of insulin-sensitizing agents may be useful in women with polycystic ovary syndrome. Copyright.COPYRGT. 2003 American Academy of Family Physicians.

L97 ANSWER 15 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 2003194005 EMBASE

TITLE: The evaluation and management of hirsutism.

AUTHOR: Azziz R.

CORPORATE SOURCE: Dr. R. Azziz, Cedars Sinai Medical Center, Dept. of Obstetrics and Gynecology, 8635 West Third Street, Los Angeles, CA 90048, United States. azzizr@cshs.org

SOURCE: Obstetrics and Gynecology, (1 May 2003) 101/5 (995-1007).

Refs: 63

ISSN: 0029-7844 CODEN: OBGNAS

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 010 Obstetrics and Gynecology  
 013 Dermatology and Venereology  
 036 Health Policy, Economics and Management  
 037 Drug Literature Index  
 038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Hirsutism is the presence of terminal (coarse) **hairs** in females in a male-like pattern, affecting between 5% and 15% of women, depending on definition. Hirsutism has a significant negative impact on psychosocial development and is usually a sign of an underlying endocrine abnormality - namely, androgen excess. The most common cause of androgen excess is the polycystic ovary syndrome (PCOS), with 21-hydroxylase-deficient nonclassic adrenal hyperplasia, the hyperandrogenic insulin-resistant acanthosis nigricans syndrome, androgen-secreting tumors, and androgenic drug intake occurring less frequently. However, although 70-80% of patients with androgen excess demonstrate hirsutism, this sign may be less prevalent among women of Asian extraction. Conversely, not all hirsute patients have evidence of detectable androgen excess, as 5-15% of these women have "idiopathic hirsutism," with normal ovulatory function and androgen levels. There is a strong familial predilection for hirsutism, primarily because the underlying endocrine disorders (eg, PCOS) and the factors regulating the development of **hair** growth (eg, androgen receptor activity, 5.alpha.-reductase activity) have a strong genetic component. The diagnostic evaluation of the potentially hirsute patient first involves confirming the presence of hirsutism and then excluding associated or etiological abnormalities and disorders (eg, ovulatory dysfunction, adrenal hyperplasia, diabetes, thyroid hormone abnormalities). Treatment should be undertaken using combination therapy, to possibly include 1) hormonal suppression (oral contraceptives, long-acting gonadotropin-releasing hormone analogues, and insulin

sensitizers), 2) peripheral androgen blockade (spironolactone, flutamide, cyproterone acetate, or finasteride), and 3) mechanical/cosmetic amelioration and destruction of the unwanted **hairs** (electrolysis and, potentially, laser **hair** removal). The application of eflornithine hydrochloride 13.9% topical cream may also be useful to ameliorate unwanted facial **hair** growth. Overall, although hirsutism is a frequent and distressing abnormality often signaling an underlying endocrine disorder, a systematic approach to evaluation will uncover the etiology, and combination therapy will provide satisfactory treatment for most patients. .COPYRGT. 2003 by The American College of Obstetricians and Gynecologists.

L97 ANSWER 16 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 2003193483 EMBASE

TITLE: Cutaneous manifestations of endocrine disorders: A guide for dermatologists.

AUTHOR: Jabbour S.A.

CORPORATE SOURCE: Dr. S.A. Jabbour, 211 South 9th Street, Philadelphia, PA 19107, United States. serge.jabbour@mail.tju.edu

SOURCE: American Journal of Clinical Dermatology, (2003) 4/5 (315-331).

Refs: 104

ISSN: 1175-0561 CODEN: AJCDCI

COUNTRY: New Zealand

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 003 Endocrinology  
013 Dermatology and Venereology  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Dermatologists may commonly see skin lesions that reflect an underlying endocrine disorder. Identifying the endocrinopathy is very important, so that patients can receive corrective rather than symptomatic treatment. Skin diseases with underlying endocrine pathology include: thyrotoxicosis; hypothyroidism; Cushing syndrome; Addison disease; acromegaly; hyperandrogenism; hypopituitarism; primary hyperparathyroidism; hypoparathyroidism; pseudohypoparathyroidism and manifestations of diabetes mellitus. Thyrotoxicosis may lead to multiple cutaneous manifestations, including **hair loss**, pretibial myxedema, onycholysis and acropachy. In patients with hypothyroidism, there is **hair loss**, the skin is cold and pale, with myxedematous changes, mainly in the hands and in the periorbital region. The striking features of Cushing syndrome are centripetal obesity, moon facies, buffalo hump, supraclavicular fat pads, and abdominal striae. In Addison disease, the skin is hyperpigmented, mostly on the face, neck and back of the hands. Virtually all patients with acromegaly have acral and soft tissue overgrowth, with characteristic findings, like macrognathia and enlarged hands and feet. The skin is thickened, and facial features are coarser. Conditions leading to hyperandrogenism in females present as acne, hirsutism and signs of virilization (temporal **balding**, clitoromegaly). A prominent feature of hypopituitarism is a pallor of the skin with a yellowish tinge. The skin is also thinner, resulting in fine wrinkling around the eyes and mouth, making the patient look older. Primary hyperparathyroidism is rarely associated with pruritus and chronic urticaria. In hypoparathyroidism, the skin is dry, scaly and puffy. Nails become brittle and **hair** is coarse and sparse. Pseudohypoparathyroidism may have a special somatic phenotype known as Albright osteodystrophy. This consists of short stature, short neck, brachydactyly and subcutaneous calcifications. Some of the cutaneous

manifestations of diabetes mellitus include necrobiosis lipoidica diabetorum, diabetic dermopathy, scleredema adultorum and acanthosis nigricans.

L97 ANSWER 17 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
 ACCESSION NUMBER: 2003047397 EMBASE  
 TITLE: Polycystic ovary syndrome: Pathogenesis and treatment over the short and long term.  
 AUTHOR: Marx T.L.; Mehta A.E.  
 CORPORATE SOURCE: Dr. A.E. Mehta, Department of Endocrinology, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, United States  
 SOURCE: Cleveland Clinic Journal of Medicine, (1 Jan 2003) 70/1 (31-45).  
 Refs: 38  
 ISSN: 0891-1150 CODEN: CCJMEL  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 003 Endocrinology  
 005 General Pathology and Pathological Anatomy  
 010 Obstetrics and Gynecology  
 016 Cancer  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB Although polycystic ovary syndrome (PCOS) is associated with hyperandrogenism and infertility early in life, it is a harbinger of a lifelong condition that can lead to serious sequelae such as endometrial or ovarian cancer, diabetes mellitus, and coronary artery disease. We review the pathophysiology, diagnosis, and treatment of this condition.

L97 ANSWER 18 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
 ACCESSION NUMBER: 2002368096 EMBASE  
 TITLE: Toward optimal health: The experts discuss polycystic ovary syndrome.  
 AUTHOR: Meisler J.G.  
 CORPORATE SOURCE: J.G. Meisler, Journal of Women's Health, Gender-Based Medicine, 31 Macopin Avenue, Montclair, NJ 07043, United States. jgmeisler@comcast.net  
 SOURCE: Journal of Women's Health and Gender-Based Medicine, (2002) 11/7 (579-584).  
 ISSN: 1524-6094 CODEN: JWHMFP  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Note  
 FILE SEGMENT: 003 Endocrinology  
 005 General Pathology and Pathological Anatomy  
 010 Obstetrics and Gynecology  
 017 Public Health, Social Medicine and Epidemiology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English

L97 ANSWER 19 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
 ACCESSION NUMBER: 2002263869 EMBASE  
 TITLE: Polycystic ovary syndrome in adolescence.  
 AUTHOR: Baumann E.E.; Rosenfield R.L.  
 CORPORATE SOURCE: Dr. E.E. Baumann, Univ. of Chicago Children's Hospital, MC 5053, 5841 S. Maryland Avenue, Chicago, IL 60637-1470, United States. ebaumann@peds.bsd.uchicago.edu  
 SOURCE: Endocrinologist, (2002) 12/4 (333-348).

Refs: 151  
 ISSN: 1051-2144 CODEN: EDOCEB

COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 003 Endocrinology  
 007 Pediatrics and Pediatric Surgery  
 010 Obstetrics and Gynecology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles

LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB Polycystic ovary syndrome (PCOS) is a syndrome of chronic androgen excess that may have its origins in childhood or even in utero. The anovulation of PCOS usually seems to be attributable to intraovarian androgen excess, which in turn arises from functional ovarian hyperandrogenism. PCOS typically appears to arise as a complex genetic disorder in which an intrinsic genetic trait interacts with other congenital or extrinsic environmental factors to cause dysregulation of steroidogenesis. Insulin-resistant hyperinsulinism related to type 2 diabetes mellitus is often an important factor in the development of PCOS. PCOS should be suspected in an adolescent female with hirsutism, acne, seborrhea, diffuse **alopecia**, hyperhidrosis, menstrual irregularity, or obesity. Any one of these may be the sole feature. The natural history of PCOS is not known with certainty; yet, intrauterine growth retardation, premature pubarche and other forms of sexual precocity, and obesity seem to be risk factors and/or antecedents of PCOS. The diagnosis is based on clinical and biochemical criteria and exclusion of other causes of hyperandrogenism. Oral contraceptive therapy is usually first-line treatment. Adolescents with PCOS are at risk for diabetes mellitus and cardiovascular disease, as are their family members.

L97 ANSWER 20 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
 ACCESSION NUMBER: 2002425268 EMBASE  
 TITLE: From **HAIR**-AN to eternity.  
 AUTHOR: Schroeder B.; Amesse L.S.; Ding X.; Pfaff-Amesse T.  
 CORPORATE SOURCE: Dr. B. Schroeder, Div. of Reproductive Endocrinology,  
 Department of Obstetrics, Wright State Univ. Sch. of  
 Medicine, Dayton, OH, United States  
 SOURCE: Journal of Pediatric and Adolescent Gynecology, (2002) 15/4  
 (235-240).  
 Refs: 13  
 ISSN: 1083-3188 CODEN: JPAGFP  
 S 1083-3188(02)00162-6  
 PUBLISHER IDENT.:  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Conference Article  
 FILE SEGMENT: 003 Endocrinology  
 007 Pediatrics and Pediatric Surgery  
 010 Obstetrics and Gynecology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English

L97 ANSWER 21 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
 ACCESSION NUMBER: 2002249763 EMBASE  
 TITLE: [The role of metformine chlorhydrate therapy in the  
 treatment of polycystic ovary syndrome (PCOS)].  
 A METFORMIN SZEREPE A PCOS KEZELESEBEN.  
 AUTHOR: Papp S.  
 CORPORATE SOURCE: Dr. S. Papp, Szuleszet-Nogyogy. Szakrendeles, Egeszsegugyi  
 KHT, Fonyod, Hungary  
 SOURCE: Magyar Noorvosok Lapja, (2002) 65/3 (201-207).

Refs: 13  
ISSN: 0025-021X CODEN: MNLAA8

COUNTRY: Hungary  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 010 Obstetrics and Gynecology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: Hungarian  
SUMMARY LANGUAGE: English; Hungarian

AB The author reports his one and a half year's experience regarding the treatment of PCOS (polycystic ovary syndrome) with the use of Metformine. The aim of this therapy is to correct disturbances induced by the compensatory hyperinsulinaemia of insulin - resistance. In cases of meeting the diagnostic criteria for PCOS and hyperinsulinaemia Metformine treatment was initiated and continued for 4-12 months. Most important criteria were represented by the characteristic sonographic appearance of the ovaries and the compensatory hyperinsulinaemia. 2. Oligo- or amenorrhoeic episodes following the menarche. Anovulation. 3. Sterility, infertility. 4. Hirsutism. **Alopecia**. 5. Obesity. 6. Acne. Acanthosis nigricans. 7. Unresponsive Clomifen test or the test leading to hyperstimulation. 8. Pathological serum-sample results: LH/ FSH ratio greater than 2.5; low progesteron, occasionally increased estrogen levels; increased testosterone levels (above 2.0 nmol/l); hyperinsulinaemia (fasting glucose/insulin ratio lower than 4.5); occasional associated hyperprolactinaemia. Since these patients were young impairment of their lipoprotein metabolism was not characteristic. The diagnosis of PCOS was established when at least two of the above listed criteria were present in association with two impaired laboratory results as well as the characteristic ultrasound image and hyperinsulinaemia. Each patient was given a detailed information about the expected duration, mode and possible side effects of the treatment as well as the essentials regarding their illness and therapy. The author avoided administration of other, hormonal drugs during the first months of Metformine therapy except in cases where a serious indication was present. Changes in the sonographic appearance of the ovaries, resulting in regular ovulatory cycles, pregnancy, normalisation of the hormonal status, as well as improvement of the various other symptoms (acne, hirsutism, obesity) were the bases of controle of the patients' condition. Two out of the 33 treated patients stopped treatment due to the side effects followed by another two after two to three months. In 5 cases where pregnancy was the main goal, regular cycles returned. 12 pregnancies resulted out of which one ectopic and one missed abortion occured. There were no cases of gestational diabetes or spontaneous abortion. By using only Metformine 7 patients with PCOS whose main problem was cycle-disturbance and didn't want pregnancy resumed regular cycles and normal laboratory values. The improvement lasted for only a few months in 5 cases followed by a relapse. It is an interesting observation that patients who strictly adhered to the dietary recommendations and were able to lose 3-8 kilogrammes of weight showed a faster and considerably longer-lasting improvement. The therapeutic efforts were often insufficient with patients unable to lose weight. The author would like to stress upon a shift in the approach of the clinical care of patients with polycystic ovary syndrome from the symptome-driven care and follow methods to primarily prevent the chronic disease which can appear in youth. Metabolic disturbances playing a determinant role in the onset of PCOS are important pathogenic factors for the early onset of carbohydrate-intolerance or diabetes. The lipoprotein lipid profiles are compatible with the effects of insulin-resistance. Disturbed cholesterol and triglyceride metabolism may initiate premature cardiovascular disease. The efficacy of prevention depends upon a well coordinated team-work. There is a need to delineate and prepare professional protocols presenting uniform guidelines and principles of care.

L97 ANSWER 22 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 2002150998 EMBASE

TITLE: Functional hyperandrogenism - Classification, etiology, diagnostic and therapy.

AUTHOR: Geithovél F.

CORPORATE SOURCE: Prof. F. Geithovél, Kaiser Joseph Strasse 168, D-79098 Freiburg, Germany. geithoevel@t-online.de

SOURCE: Therapeutische Umschau, (2002) 59/4 (163-173).

Refs: 25

ISSN: 0040-5930 CODEN: THUMAM

COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology  
010 Obstetrics and Gynecology  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The classification of functional hyperandrogenism (FHA) presented in this paper is based on well known clinical experience supported by recent data of molecular biology. Funktional hyperandrogenism is composed of various organ systemspecific entities with consequently differential diagnostic and therapeutic strategies. The term polycystic ovary syndroms (PCOS) is misleading and should be replaced by adequate descriptions. In spite of intense discussions and progress in molecular biology are with the exception of the here described FHA III-group the etiological consequences unresolved in terms of diagnostic and therapeutic procedures. Based on recent findings on the human genome genetic screening methods (Microarrays) may be available in the near future to allow a better understanding of the underlying pathophysiology.

L97 ANSWER 23 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 2002159187 EMBASE

TITLE: Hirsutism.

AUTHOR: Gilling-Smith C.

CORPORATE SOURCE: C. Gilling-Smith, Conception Unit, Chelsea and Westminster Hospital, 369 Fulham Road, London SW10 9NH, United Kingdom. cgs@chelwest.nhs.uk

SOURCE: Current Obstetrics and Gynaecology, (2002) 12/3 (144-149).

ISSN: 0957-5847 CODEN: COGYFP

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 003 Endocrinology  
005 General Pathology and Pathological Anatomy  
010 Obstetrics and Gynecology  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Hirsutism is defined as the excessive growth of terminal **hair** on the face and body of a female in atypical male pattern distribution. Untreated it can be associated with considerable loss of self-esteem and psychological morbidity. Hyperandrogenaemia is the key trigger for excess **hair** growth but the expression and severity are modified by genetic factors, such as sensitivity of the **hair** follicle to androgens, and metabolic factors, in particular body weight and hyperinsulinaemia. Polycystic ovary syndrome, resulting in excess ovarian androgen production, is the most common cause of hirsutism. A raised serum testosterone level of > 5 nmol/l should prompt further investigations to exclude adrenal pathology or underlying androgen-secreting tumour. Treatment depends on the underlying cause. In women with polycystic ovary syndrome or idiopathic hirsutism, cyproterone acetate prescribed in a

reversed sequential regimen with oestradiol is a very effective first-line treatment. Metformin is a useful second line approach in women with poor tolerance or poor response to cyproterone acetate. In all cases, weight reduction to achieve a normal body mass index is critical to achieving effective therapy. .COPYRGHT. 2002 Elsevier Science Ltd.

L97 ANSWER 24 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
 ACCESSION NUMBER: 2002269378 EMBASE  
 TITLE: The unfolding story of polycystic ovary syndrome.  
 AUTHOR: Ilbery M.  
 CORPORATE SOURCE: Dr. M. Ilbery, Queensland Fertility Group, Wickham Terrace,  
 Brisbane, QLD, Australia  
 SOURCE: Medicine Today, (2002) 3/7 (20-27).  
 ISSN: 1443-430X CODEN: MTNBCV  
 COUNTRY: Australia  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 003 Endocrinology  
 005 General Pathology and Pathological Anatomy  
 010 Obstetrics and Gynecology  
 022 Human Genetics  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB .bul. Polycystic ovary syndrome (PCOS) is the commonest endocrine problem for women, occurring in 5 to 10% of premenopausal women. .bul. A 'polycystic ovarian' ultrasound pattern occurs as an incidental finding in about 20% of the normal female population. .bul. PCOS is a heterogenous clinical picture, characterised by the association of menstrual abnormality (due to chronic anovulation), obesity and hyperandrogenism. .bul. About 40% of women with PCOS are obese. Weight loss is the first line of therapy for regulating menstruation, reducing body **hair** in hirsutism and inducing ovulation in fertility therapy. .bul. About 30 to 60% of women with PCOS have insulin resistance and hyperinsulinaemia, and are at risk of developing type 2 diabetes mellitus. .bul. Although there is much observational evidence, there is, as yet, no definitive high quality evidence to support the use of metformin in treating PCOS. Definitive studies are needed to assess its use in anovulation, and for women with androgen excess and vascular risk factors.

L97 ANSWER 25 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
 ACCESSION NUMBER: 2002064794 EMBASE  
 TITLE: American association of clinical endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of hyperandrogenic disorders.  
 SOURCE: Endocrine Practice, (2001) 7/2 (121-134).  
 Refs: 86  
 ISSN: 1530-891X CODEN: EPNRAT  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 003 Endocrinology  
 006 Internal Medicine  
 010 Obstetrics and Gynecology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English

L97 ANSWER 26 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
 ACCESSION NUMBER: 2001040723 EMBASE  
 TITLE: Tackling polycystic ovary syndrome.  
 SOURCE: Drug and Therapeutics Bulletin, (2001) 39/1 (1-5).

Refs: 24

ISSN: 0012-6543 CODEN: DRTBAE

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 010 Obstetrics and Gynecology

017 Public Health, Social Medicine and Epidemiology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Up to one-third of women in the UK have polycystic ovaries (i.e. 10 or more follicles per ovary detected on ultrasound). (1) An estimated one-third of these women have polycystic ovary syndrome, (2) usually defined in the UK as polycystic ovaries together with one or more characteristic features (hirsutism, male-pattern **baldness**, acne, oligomenorrhoea or amenorrhoea, obesity, or raised serum concentrations of testosterone and/or luteinizing hormone [LH]). (3) The metabolic abnormalities often associated with polycystic ovary syndrome (insulin resistance and abnormal serum lipid concentrations) also put some women with the syndrome at increased risk of developing diabetes mellitus. (4) Here, we review the management of women with polycystic ovary syndrome.

L97 ANSWER 27 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 2002234357 EMBASE

TITLE: The SAHA syndrome.

AUTHOR: Orfanos C.E.; Adler Y.D.; Zouboulis C.C.

CORPORATE SOURCE: Dr. C.C. Zouboulis, Department of Dermatology, Univ. Med. Center Benjamin Franklin, Free University of Berlin, Fabeckstrasse 60-62, D-14195 Berlin, Germany.  
zouboulis@medizin.fu-berlin.de

SOURCE: Hormone Research, (2000) 54/5-6 (251-258).

Refs: 69

ISSN: 0301-0163 CODEN: HRMRA3

COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 003 Endocrinology

010 Obstetrics and Gynecology

013 Dermatology and Venereology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The presence of seborrhoea, acne, hirsutism and **alopecia** in women has first been summarized as SAHA syndrome in 1982 and can be associated with polycystic ovary syndrome, cystic mastitis, obesity and infertility. In 1994, the association of these androgen-dependent cutaneous signs, was classified according to their etiology into four types: (1) idiopathic, (2) ovarian, (3) adrenal, and (4) hyperprolactinemic SAHA. The HAIRAN syndrome has been currently described as a fifth variant with polyendocrinopathy. The SAHA syndrome generally occurs in young to middle-aged women and involves either the presence of elevated blood levels of androgens or increased androgen-driven peripheral response with normal circulating androgen levels. Peripheral metabolism of androgens takes place in various areas within the pilosebaceous unit, as indicated by local differences in the activities of aromatase, 5.alpha.-reductase as well as of the presence of the androgen receptors. In cases of SAHA syndrome, careful diagnostic and clinical evaluation has to be performed in order to identify the cause for peripheral hyperandrogenism and to exclude androgen-producing tumors. Treatment will target the etiology, whereas the management in idiopathic cases will aim to improve the clinical features of SAHA. Copyright .COPYRGT. 2001 S. Karger AG, Basel.

L97 ANSWER 28 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
ACCESSION NUMBER: 1999190394 EMBASE  
TITLE: Acute diffuse telogen **hair loss**.  
AUTHOR: Sinclair R.  
CORPORATE SOURCE: Dr. R. Sinclair, Department of Medicine, St Vincent's  
Hospital, Fitzroy, Vic. 3065, Australia  
SOURCE: International Journal of Dermatology, (1999) 38/SUPPL. 1  
(8-18).  
Refs: 32  
ISSN: 0011-9059 CODEN: IJDEBB  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 013 Dermatology and Venereology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English

L97 ANSWER 29 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
ACCESSION NUMBER: 97184738 EMBASE  
DOCUMENT NUMBER: 1997184738  
TITLE: Pentosan polysulfate sodium and midodrine hydrochloride.  
AUTHOR: Levien T.; Baker D.E.  
CORPORATE SOURCE: T. Levien, Drug Information Center, College of Pharmacy,  
Washington State University, 601 West First Avenue,  
Spokane, WA 99204-0399, United States  
SOURCE: Hospital Pharmacy, (1997) 32/6 (884-898).  
Refs: 28  
ISSN: 0018-5787 CODEN: HOPHAZ  
COUNTRY: United States  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 006 Internal Medicine  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English

L97 ANSWER 30 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN  
ACCESSION NUMBER: 79226706 EMBASE  
DOCUMENT NUMBER: 1979226706  
TITLE: The proof of drug effects of endocrine glands or endocrine  
target organs by means of toxicological investigations.  
AUTHOR: Kramer M.; Guenzel P.  
CORPORATE SOURCE: Hoechst AG, Frankfurt/M., Germany  
SOURCE: Pharmacology and Therapeutics, (1979) 5/1-3 (287-296).  
CODEN: PHTHDT  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 037 Drug Literature Index  
030 Pharmacology  
038 Adverse Reactions Titles  
003 Endocrinology  
LANGUAGE: English

AB During the preclinical safety evaluation of new drugs, animal studies with  
repeated administration of the new compound of different duration are  
normally carried out. These studies are routinely done in rats and dogs  
but very often other species - mice, rabbits, or even monkeys - are  
additionally included. In respect to drug effects on sexual glands or  
respective target organs reproduction tests will give further information.

L97 ANSWER 31 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
ACCESSION NUMBER: 2003:343802 BIOSIS

DOCUMENT NUMBER: PREV200300343802  
TITLE: Low-dose **flutamide-metformin** therapy  
reverses: Insulin resistance and reduces fat mass in  
nonobese adolescents with ovarian hyperandrogenism.  
AUTHOR(S): Ibanez, Lourdes (1); Ong, Ken; Ferrer, Angela; Amin,  
Rakesh; Dunger, David; de Zegher, Francis  
CORPORATE SOURCE: (1) Endocrinology Unit, Hospital Sant Joan de Deu,  
University of Barcelona, Passeig de Sant Joan de Deu, 2,  
Esplugues, Barcelona, 08950, Spain: libanez@hsjdbcn.org  
Spain  
SOURCE: Journal of Clinical Endocrinology & Metabolism, (June 2003,  
2003) Vol. 88, No. 6, pp. 2600-2606. print.  
ISSN: 0021-972X.  
DOCUMENT TYPE: Article  
LANGUAGE: English

AB Ovarian hyperandrogenism is a common disorder often presenting post  
menarche with anovulatory oligomenorrhea and signs of androgen excess.  
Associated hyperinsulinemic insulin resistance, dyslipidemia, and central  
fat excess herald long-term disease risk. Combined antiandrogen (  
**flutamide** 250 mg/d) and insulin-sensitizing (**metformin**)  
therapy has beneficial effects, in particular on dyslipidemia and androgen  
excess in young women. We studied the effects of low-dose  
**flutamide-metformin** combination on metabolic variables  
and body composition in adolescent girls with ovarian hyperandrogenism.  
Thirty teenage girls (age range, 13.6-18.6 yr) with hyperinsulinemic  
hyperandrogenism participated in a 12-month pilot study with a 3-month  
off-treatment phase and a 9-month treatment phase (randomized sequence) on  
combined **flutamide** (125 mg/d) and **metformin** (1275  
mg/d). Body composition was assessed by dual-energy x-ray absorptiometry;  
endocrine-metabolic state and ovulation rate were screened every 3 months.  
Insulin sensitivity was assessed by homeostasis model assessment (HOMA).  
Overnight GH and LH profiles were obtained pretreatment and after 6 months  
on treatment (n=8). Over the 3-month pretreatment control phase (n=14) all  
study indices were unchanged. **Flutamide-metformin**  
treatment (n=30) was followed within 3 months by marked decreases in  
**hirsutism** score and serum androgens, by a more than 50% increase  
in insulin sensitivity and by a less atherogenic lipid profile (all  
P<0.0001). After 9 months on **flutamide-metformin**, body  
fat decreased by 10%, with a preferential 20% loss of abdominal fat;  
conversely lean body mass increased, and total body weight remained  
unchanged; ovulation rate increased from 7-87% after 9 months. Baseline GH  
hypersecretion and elevated serum IGF-1 normalized after 6 months on  
**flutamide-metformin**. Within 3 months post treatment  
(n=16), a rebound was observed for all assessed indices. In conclusion, in  
teenage girls with ovarian hyperandrogenism, low-dose combined  
**flutamide-metformin** therapy attenuated a spectrum of  
abnormalities, including insulin resistance and hyperlipidemia. Improved  
insulin sensitivity and reduced androgen activity led to a marked  
redistribution of body fat and lean mass, resulting in a more feminine  
body shape.

L97 ANSWER 32 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:401578 BIOSIS  
DOCUMENT NUMBER: PREV200200401578  
TITLE: Additive effects of insulin-sensitizing and anti-androgen  
treatment in young, nonobese women with hyperinsulinism,  
hyperandrogenism, dyslipidemia, and anovulation.  
AUTHOR(S): Ibanez, Lourdes (1); Valls, Carme; Ferrer, Angela; Ong,  
Ken; Dunger, David B.; de Zegher, Francis  
CORPORATE SOURCE: (1) Endocrinology Unit, Hospital Sant Joan de Deu,  
University of Barcelona, Passeig de Sant Joan de Deu, 2,

SOURCE: Esplugues, 08950, Barcelona: libanez@hsjdbcn.org Spain  
Journal of Clinical Endocrinology & Metabolism, (June, 2002) Vol. 87, No. 6, pp. 2870-2874.  
http://jcem.endojournals.org. print.  
ISSN: 0021-972X.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The endocrine-metabolic hallmarks of polycystic ovary syndrome are hyperinsulinism, hyperandrogenism, dyslipidemia, and anovulation. We hypothesized that dyslipidemia and anovulation in nonobese women with polycystic ovary syndrome are essentially secondary to the concerted effects of hyperandrogenism and insulin resistance. We tested this hypothesis by comparing the efficacy of anti-androgen (**flutamide**) or insulin-sensitizing (**metformin**) monotherapy to that of combined therapy in normalizing the endocrine-metabolic and anovulatory status of nonobese, young women with hyperinsulinemic hyperandrogenism. Thirty-one young women (mean age, 18.7 yr; body mass index, 21.9 kg/m<sup>2</sup>; **hirsutism** score, 16; monthly ovulation rate monitored by weekly serum **progesterone**, 10%) were randomly assigned to receive once daily **flutamide** (250 mg; n = 10), **metformin** (1275 mg; n = 8), or combined flutamidemetformin therapy (n = 13) for 9 months. At baseline, there were no endocrine-metabolic differences among treatment groups. Compared with monotherapy, combined flutamidemetformin therapy resulted in greater improvements in insulin sensitivity, in testosterone, androstenedione, dehydroepiandrosterone sulfate, and triglyceride levels, and in low-density lipoprotein/high-density lipoprotein-cholesterol ratio (all  $P < 0.005$ ). Monthly ovulation rates increased after 9 months to 75 and 92%, respectively, with **metformin** alone or with combined therapy, but were unimproved with **flutamide** alone. All treatments were well tolerated. In conclusion, combined anti-androgen and insulin-sensitizing treatment in young, nonobese women with hyperinsulinemic hyperandrogenism had additive benefits on insulin sensitivity, hyperandrogenemia, and dyslipidemia. The data from this small study suggest that dyslipidemia is secondary to excess androgen action in concert with the hyperinsulinemia associated with insulin resistance. In contrast, anovulation seems to be mainly attributable to insulin resistance and hyperinsulinemia.

L97 ANSWER 33 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:566797 BIOSIS

DOCUMENT NUMBER: PREV200200566797

TITLE: [**Hirsutism** and hypertrichosis in adults: Investigations and treatment.  
Original Title: Hypertrichose et **hirsutisme**.  
Demarche diagnostique et therapeutique chez l'adulte..

AUTHOR(S): Bennet, A. (1)

CORPORATE SOURCE: (1) Service d'Endocrinologie, Hopital de Rangueil, CHU de Toulouse, 31403, Toulouse Cedex 4 France

SOURCE: Annales de Dermatologie et de Venereologie, (Mai, 2002)  
Vol. 129, No. 5 Cahier 2, pp. 804-812. print.  
ISSN: 0151-9638.

DOCUMENT TYPE: Article

LANGUAGE: French

AB Hypertrichosis, characterized by increased **hair** growth located in non-androgen-dependent areas, does not justify the monitoring of hormone levels, conversely to **hirsutism**, with increased **hair** growth in androgen-dependent areas of the female genitals. Adult hypertrichosis is iatrogenic (minoxidil, ciclosporine, diazoxide or glucocorticosteroids), of metabolic origin (porphyria), nutritional (anorexia) or paraneoplastic (hypertrichosis lanuoginosa). Metabolic or general assessment can help clinical diagnosis. In non-iatrogenic

**hirsutism** the following must be eliminated: 1) a virilizing tumor (ovarian, adrenal) when confronted with rapid progression or recent **hirsutism**, plasma testosterone (T) >1.5 ng/ml and/or (adrenal tumor) DHEA-sulfate (DHEAS) >700 mug/dl and associated with hypertension; 2) when confronted with characteristic signs of **hirsutism**, Cushing's syndrome (post-dexamethasone cortisol), hyperprolactinemia (pooled PRL), or acromegalia (IGF1). Measurement of 17-OH-**progesterone** at 8 am on the 4th day of the cycle detects the "late manifestation" homozygous forms of a 21-hydroxylase (21OHD) block. The more frequent forms are: 1) ovarian polymicrocystic or **hirsutism**-anovulation syndromes without other causes (LH/FSH, T, hyperinsulinemia, sonography); 2) functional adrenal hyperandrogenia (increased DHEAS without organic cause); 3) idiopathic **hirsutism**. Treatment can be local (discoloration, depilation, diathermo-coagulation, laser). Treatment of **hirsutism** of organic origin is etiologic. The inhibitory effects of glucocorticosteroids are mediated by 21OHD. The most effective treatments are anti-androgenic: **cyproterone acetate**, **progesterone**-like and anti-gonadotropic (contraceptive) agents; and the only product in France officially indicated in "**hirsutism**", **spironolactone** (anti-mineralocorticosteroid); and **flutamide**, pure anti-androgen (probably hepatotoxic). Finasteride (type II 5 alpha-reductase inhibitor) appears less effective. Estrogen-progestagen-like agents can be associated with anti-androgens. We should also mention the GnRH-agonists, and finally, dietetics and **metformine** (in cases of insulin-resistance).

L97 ANSWER 34 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 ACCESSION NUMBER: 2002:503587 BIOSIS  
 DOCUMENT NUMBER: PREV200200503587  
 TITLE: **Flutamide** (F) and **metformin** (M) added  
 to low-calorie diet (LCD) in the treatment of obese women  
 with PCOS.  
 AUTHOR(S): Gambineri, A. (1); Pelusi, C. (1); Vicennati, V. (1);  
 Pagotto, U. (1); Pasquali, R. (1)  
 CORPORATE SOURCE: (1) Endocrinology Unit, University of Bologna, Bologna  
 Italy  
 SOURCE: International Journal of Obesity, (August, 2002) Vol. 26,  
 No. Supplement 1, pp. S81. <http://www.naturesj.com/ijo/index.html>. print.  
 Meeting Info.: Ninth International Congress on Obesity Sao  
 Paulo, Brazil August 24-29, 2002  
 ISSN: 0307-0565.  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

L97 ANSWER 35 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 ACCESSION NUMBER: 2002:568747 BIOSIS  
 DOCUMENT NUMBER: PREV200200568747  
 TITLE: Insulin resistance and hyperandrogenemia. The impact of  
**metformin** therapy.  
 AUTHOR(S): Helmer, R. (1); Terkamp, C. (1); von zur Muehlen, A. (1);  
 Brabant, G. (1); Schoefl, C. (1)  
 CORPORATE SOURCE: (1) Abt. Klinische Endokrinologie, Medizinische Hochschule  
 Hannover, Hannover Germany  
 SOURCE: Diabetologia, (August, 2001) Vol. 44, No. Supplement 1, pp.  
 A187. print.  
 Meeting Info.: 37th Annual Meeting of the European  
 Association for the Study of Diabetes Glasgow, Scotland, UK  
 September 09-13, 2001 European Association for the Study of  
 Diabetes

. ISSN: 0012-186X.  
DOCUMENT TYPE: Conference  
LANGUAGE: English

L97 ANSWER 36 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
ACCESSION NUMBER: 2000:461618 BIOSIS  
DOCUMENT NUMBER: PREV200000461618  
TITLE: Endocrine and metabolic effects of **metformin**  
versus ethinyl estradiol-**cyproterone**  
**acetate** in obese women with polycystic ovary  
syndrome: A randomized study.  
AUTHOR(S): Morin-Papunen, Laure C.; Vauhkonen, Ilkka; Koivunen, Riitta  
M.; Ruukonen, Aimo; Martikainen, Hannu K.; Tapanainen, Juha  
S. (1)  
CORPORATE SOURCE: (1) Department of Obstetrics and Gynecology, University  
Hospital of Oulu, Kajaanintie 52 A, FIN-90220, Oulu  
Finland  
SOURCE: Journal of Clinical Endocrinology & Metabolism, (September,  
2000) Vol. 85, No. 9, pp. 3161-3168. print.  
ISSN: 0021-972X.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB **Metformin**, a **biguanide** antihyperglycemic drug, has  
been shown to improve ovarian function and glucose metabolism in women  
with polycystic ovary syndrome (PCOS), but results concerning its effects  
on insulin sensitivity are controversial. Oral contraceptive pills are  
commonly used in the treatment of PCOS; but, like **metformin**,  
their influence on insulin sensitivity is not well known. We randomized 32  
obese (body mass index > 27 kg/m<sup>2</sup>) women with PCOS, either to  
**metformin** (500 mg X 2 daily for 3 months, then 1000 mg X 2 daily  
for 3 months) or to ethinyl estradiol (35 mug)-**cyproterone**  
**acetate** (2 mg) oral contraceptive pills (Diane Nova) for 6 months.  
**Metformin** significantly decreased the waist-to-hip ratio, serum  
testosterone, fasting free fatty acid, and insulin concentrations and  
improved oxidative glucose utilization and menstrual cyclicity, with  
slight (but nonsignificant) improvements in insulin hepatic extraction and  
insulin sensitivity. Diane Nova significantly decreased serum testosterone  
and increased serum sex hormone-binding globulin concentrations and  
glucose area under the curve during oral glucose tolerance test. It is  
concluded that **metformin**, probably by way of its effect on  
adipose tissue, leads to reduction of hyperinsulinemia and concomitant  
improvement in the menstrual pattern; and therefore, it offers a useful  
alternative treatment for obese, anovulatory women with PCOS. Despite  
slight worsening of glucose tolerance, Diane Nova is an efficient  
treatment for women with hyperandrogenism and **hirsutism**.

L97 ANSWER 37 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
ACCESSION NUMBER: 2001:147375 BIOSIS  
DOCUMENT NUMBER: PREV200100147375  
TITLE: Effect of long-term treatment with **metformin**  
added to hypocaloric diet on body composition, fat  
distribution, and androgen and insulin levels in  
abdominally obese women with and without the polycystic  
ovary syndrome.  
AUTHOR(S): Pasquali, Renato (1); Gambineri, Alessandra; Biscotti,  
Domenico; Vicennati, Valentina; Gagliardi, Lorenza;  
Colitta, Donatella; Fiorini, Stefania; Cognigni, Graciela  
Estela; Filicori, Marco; Morselli-Labate, Antonio Maria  
CORPORATE SOURCE: (1) Endocrine Unit, Department of Internal Medicine and  
Gastroenterology, S. Orsola-Malpighi Hospital, Via

Massarenti 9, 40138, Bologna: rpasqual@almadns.unibo.it  
Italy

SOURCE: Journal of Clinical Endocrinology & Metabolism, (August, 2000) Vol. 85, No. 8, pp. 2767-2774. print.  
ISSN: 0021-972X.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Abdominal obesity and hyperinsulinemia play a key role in the development of the polycystic ovary syndrome (PCOS). Dietary-induced weight loss and the administration of insulin-lowering drugs, such as **metformin**, are usually followed by improved hyperandrogenism and related clinical abnormalities. This study was carried out to evaluate the effects of combined hypocaloric diet and **metformin** on body weight, fat distribution, the glucose-insulin system, and hormones in a group of 20 obese PCOS women (body mass index (BMI) > 28 kg/m<sup>2</sup>) with the abdominal phenotype (waist to hip ratio >0.80), and an appropriate control group of 20 obese women who were comparable for age and pattern of body fat distribution but without PCOS. At baseline, we measured sex hormone, sex hormone-binding globulin (SHBG), and leptin blood concentrations and performed an oral glucose tolerance test and computerized tomography (CT) at the L4-L5 level, to measure sc adipose tissue area (SAT) and visceral adipose tissue area. All women were then given a low-calorie diet (1200-1400 kcal/day) alone for one month, after which anthropometric parameters and CT scan were newly measured. While continuing dietary treatment, PCOS women and obese controls were subsequently placed, in a random order, on **metformin** (850 mg/os, twice daily) (12 and 8, respectively) or placebo (8 and 12, respectively), according to a double-blind design, for the following 6 months. Blood tests and the CT scan were performed in each woman at the end of the study while they were still on treatment. During the treatment period, 3 women of the control group (all treated with placebo) were excluded because of noncompliance; and 2 PCOS women, both treated with **metformin**, were also excluded because they became pregnant. Therefore, the women cohort available for final statistical analysis included 18 PCOS (10 treated with **metformin** and 8 with placebo) and 17 control women (8 treated with **metformin** and 9 with placebo). The treatment was well tolerated. In the PCOS group, **metformin** therapy improved **hirsutism** and menstrual cycles significantly more than placebo. Baseline anthropometric and CT parameters were similar in all groups. Hypocaloric dieting for 1 month similarly reduced BMI values and the waist circumference in both PCOS and control groups, without any significant effect on CT scan parameters. In both PCOS and control women, however, **metformin** treatment reduced body weight and BMI significantly more than placebo. Changes in the waist-to-hip ratio values were similar in PCOS women and controls, regardless of pharmacological treatment. **Metformin** treatment significantly decreased SAT values in both PCOS and control groups, although only in the latter group were SAT changes significantly greater than those observed during the placebo treatment. On the contrary, visceral adipose tissue area values significantly decreased during **metformin** treatment in both PCOS and control groups, but only in the former was the effect of **metformin** treatment significantly higher than that of placebo. Fasting insulin significantly decreased in both PCOS women and controls, regardless of treatment, whereas glucose-stimulated insulin significantly decreased only in PCOS women and controls treated with **metformin**. Neither **metformin** or placebo significantly modified the levels of LH, FSH, dehydroepiandrosterone sulphate, and **progesterone** in any group, whereas testosterone concentrations decreased only in PCOS women treated with **metformin**. SHBG concentrations remained unchanged in all PCOS women; whereas in the control group, they

L2 1 ANSWERS CAPLUS COPYRIGHT 2003 ACS on STN  
IC ICM A61K031-00  
CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1, 2, 62  
TI Methods and compositions based on insulin-sensitivity increasing substances for the treatment of alopecia and other disorders of the pilosebaceous apparatus  
ST biguanide inositol thiazolidinedione insulin sensitivity alopecia; oral biguanide inositol thiazolidinedione alopecia; topical biguanide inositol thiazolidinedione alopecia; hair growth promoter biguanide inositol thiazolidinedione  
IT Skin, disease  
(acanthosis nigricans; compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT Androgen receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(blockers; compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT Acne  
Alopecia  
Anti-inflammatory agents  
Antidiabetic agents - **ISIS**  
Hirsutism  
Permeation enhancers -  
Surfactants  
Vasodilators  
(compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT Drug delivery systems  
(gels; compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT Hair preparations  
(growth stimulants; compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT Skin, disease  
(ichthyosis, migratory; compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT Drug delivery systems  
(ointments, creams; compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT Drug delivery systems  
(oral; compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT Enzymes, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(steroidogenic, inhibitors or inducers; compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT Drug delivery systems  
(tinctures; compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT Drug delivery systems  
(topical; compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)  
IT 67-68-5, Dimethyl sulfoxide, biological studies 872-50-4,  
N-Methylpyrrolidone, biological studies 3079-28-5, Decylmethyl sulfoxide

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L25: Entry 3 of 5

File: USPT

Sep 12, 2000

DOCUMENT-IDENTIFIER: US 6117429 A

TITLE: Compositions and treatments for reducing potential unwanted side effects associated with long-term administration of androgenic testosterone precursors

Abstract Text (1):

A method for reducing potential adverse effects of androgenic testosterone precursors by interfering with production or action of testosterone and estrogen metabolites by nutrient combinations is described. Although androgenic testosterone precursors themselves have little or no toxicity, there is the potential for their metabolites, estradiol and dihydrotestosterone, to enhance or cause hormone-responsive illnesses such as breast or prostatic cancer, benign prostatic hyperplasia, or hirsutism or acne in women. The use of the invented nutrient combinations reduces the formation or action of estradiol and dihydrotestosterone, thereby reducing potential adverse effects from increased production of these hormones following androgenic testosterone precursor administration. This may be accomplished without negating the effects of testosterone on muscle anabolism. The nutrient combinations include androstenedione, DHEA, pregnenolone, androstenediols, norandrostenedione and norandrostenediols, and natural products which reduce estrogen effects in the estrogen-responsive tissues, and substances to reduce formation of dihydrotestosterone from testosterone in prostate tissue.

Other Reference Publication (23):

Crave, Jean-Charles, Fimbel, Sylvie, Lejeune, Herve, Cugnardney, Nathalie, Dechaud, Henri, and Pugeat, Michael. Effects of Diet and Metformin Administration on Sex Hormone-Binding Globulin, Androgens, and Insulin in Hirsute and Obese Women. Journal of Clinical Endocrinology and Metabolism, vol. 80, No. 7 (1995), pp. 2057-2062.

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L2 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 DUPLICATE 2  
 AN 1995:370284 BIOSIS  
 DN PREV199598384584  
 TI Effects of diet and **metformin** administration on sex  
 hormone-binding globulin, androgens, and insulin in **hirsute** and  
 obese women.  
 AU Crave, Jean-Charles (1); Fimbel, Sylvie; Lejeune, Herve; Cugnardey,  
 Nathalie; Dechaud, Henri; Pugeat, Michel  
 CS (1) Lab. Clin. Endocrinol., Hopital Antiquaille, 1 rue Antiquaille, 69321  
 Lyon Cedex 05 France  
 SO Journal of Clinical Endocrinology & Metabolism, (1995) Vol. 80, No. 7, pp.  
 2057-2062.  
 ISSN: 0021-972X.  
 DT Article  
 LA English  
 AB Evidence suggests that hyperinsulinemic insulin resistance may increase  
 serum levels of ovarian androgens and reduce sex hormone-binding globulin  
 (SHBG) levels in humans. The present study was conducted to assess the  
 effect of administration of the biguanide metformin, a drug commonly used  
 in the treatment of diabetes mellitus, on androgen and insulin levels in  
 24 hirsute patients. The patients selected for the study were obese, with  
 a body mass index higher than 25 kg/m<sup>2</sup> and high fasting insulin (gt 90  
 pmol/L) and low SHBG levels (lt 30 nmol/L). All patients were given a low  
 calorie diet (1500 Cal/day) and randomized for either metformin  
 administration at a dose of 850 mg or a placebo, twice daily for 4 months,  
 in a double blind study. In the placebo group, diet resulted in a  
 significant decrease in body mass index (30.8 +- 1.0 vs. 32.7 +- 1.5  
 kg/m<sup>2</sup>; P lt 0.0001), fasting insulin (127 +- 11 vs. 156 +- 14 pmol/L; P  
 lt 0.01), non-SHBG-bound testosterone (0.19 +- 0.02 vs. 0.28 +- 0.03  
 nmol/L; P lt 0.02), androstenedione (5.8 +- 0.5 vs. 9.0 +- 1.1 nmol/L; P  
 lt 0.03), and 3-alpha-diolglucuronide (8.6 +- 1.1 vs. 11.7 +- 1.9; P lt  
 0.005) plasma concentrations and a significant increase in the  
 glucose/insulin ratio (0.047 +- 0.005 vs. 0.035 +- 0.003; P lt 0.001) and  
 plasma concentrations of SHBG (26.0 +- 3.3 vs. 19.1 +- 1.9 nmol/L; P lt  
 0.001) and dehydroepiandrosterone sulfate (8.7 +- 1.5 vs. 8.4 +- 1.3; P lt  
 0.05). Beneficial effects of diet were not significantly different in the  
 patients who were given metformin instead of placebo. These results  
 confirm that weight loss induced by a low calorie diet is effective in  
 improving hyperinsulinemia and hyperandrogenism in obese and hirsute  
 women. With our study design, metformin administration had no additional  
 benefit over the effect of diet.  
 TI Effects of diet and **metformin** administration on sex  
 hormone-binding globulin, androgens, and insulin in **hirsute** and  
 obese women.

AN 97:331058 NLDB  
TI DERMATOLOGY: Excess Hair  
SO Harvard Women's Health Watch, (1 Sep 1997) Vol. 5, No. 1.  
ISSN: 1070-910X.  
PB Harvard Medical School Health Publications Group  
DT Newsletter  
LA English  
WC 1755

TX Although a luxuriant head of **hair** is often treasured, a profusion of body **hair** is another matter altogether. **Hair** on a woman's arms, legs, and face is viewed differently by various cultures and among individuals, but any growth that is heavier than average is usually a cause of cosmetic concern. While excess **hair** is occasionally a sign of an underlying medical condition, in most cases, it is nothing more than a physical trait with no health significance whatsoever.

The biology of **hair** growth The texture of **hair** that grows on any part of the body changes over a lifetime. The fine, white hairs that cover most of the body before puberty are called vellus hairs. In late childhood, the adrenal glands begin to produce androgens, which convert a percentage of those hairs to coarser, pigmented terminal hairs similar to those on the scalp. After puberty, the ovaries add to the androgen load, and additional terminal hairs may appear. Body **hair** generally gets thicker until menopause, when it gradually begins to thin. In contrast, facial **hair** often increases after menopause.

The proportion of terminal hairs at any time of life depends not only on the amount of androgen in circulation, but also on the activity in the skin of the enzyme 5-alpha reductase, which converts androgens to their active forms. One of the forms most important to **hair** growth is dihydrotestosterone (DHT). When 5-alpha reductase is activated, DHT levels rise. High DHT levels not only result in the growth of facial **hair**, but also in the loss of scalp **hair**.

Causes of excessive **hair** Excessive **hair** growth is usually classified as either hypertrichosis or **hirsutism**. Hypertrichosis is an increase in **hair** growth that is not dependent on androgens; **hirsutism** is androgen-dependent. Both can be hereditary or the result of an environmental influence; both can affect the entire body or be limited to certain areas.

Hypertrichosis usually refers to the excessive growth of vellus hairs, although it also applies to terminal hairs that emanate from moles. Having hypertrichosis usually means having a thick coat of "down" or "peach fuzz." Vellus **hair** can spring up in response to a number of conditions-nutritional disorders such as anorexia, malnutrition, or malabsorption; diseases of the nervous system like multiple sclerosis and encephalitis; an injury or fracture of an arm or leg; and even, in rare cases, to certain cancers. Hypertrichosis should disappear when the underlying condition is successfully treated.

**Hirsutism** is the growth of terminal, often whisker-like, **hair** in a normally male pattern. **Hair** can appear on the face, chest, or lower abdomen, yet, at the same time, scalp **hair** can thin out. **Hirsutism** may be due to disorders that produce abnormal amounts of androgen in either the ovaries or the adrenal glands. These include polycystic ovary disease, insulin resistance, ovarian tumors, adrenal tumors, and Cushing's disease. Increased production of prolactin-a pituitary hormone that stimulates the adrenal glands in addition to triggering the production of breast milk-and luteinizing hormone-which influences the production of ovarian androgens-can also lead to **hirsutism**. Occasionally the use of drugs, such as

**End of Result Set**

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L25: Entry 5 of 5

File: USPT

Oct 26, 1999

DOCUMENT-IDENTIFIER: US 5972944 A

TITLE: Use of thiazolidinedione derivatives in the treatment of anovulation, hyperandrogenism and hirsutismAbstract Text (1):

The present invention provides methods of using thiazolidinone derivatives to treat anovulation, hyperandrogenism and hirsutism.

Brief Summary Text (15):

Failure to treat NIDDM can result in mortality due to cardiovascular disease and in other diabetic complications including retinopathy, nephropathy, and peripheral neuropathy. For many years treatment of NIDDM has involved a program aimed at lowering blood sugar with a combination of diet and exercise. Alternatively, treatment of NIDDM involved oral hypoglycemic agents, such as sulfonylureas alone or in combination with insulin injections. Recently, alpha-glucosidase inhibitors, such as acarbose, have been shown to be effective in reducing the postprandial rise in blood glucose (Lefevre et al., Drugs, 1992;44:29-38). In Europe and Canada another treatment used primarily in obese diabetics is metformin, a biguanide.

Brief Summary Text (18):

Regarding prevention of NIDDM, there has been one disclosure of this concept using a sulfonylurea as a treatment, but this concept is not highly regarded in the scientific community because prolonged treatment with sulfonylureas can reduce insulin secretion by destroying the pancreatic beta cells. Moreover, sulfonylureas can cause clinically severe hypoglycemia. The concept of using a biguanide, such as metformin, has also been disclosed.

## CLAIMS:

7. A method of treating hirsutism, the method comprising administering to a patient suffering from hirsutism a therapeutically effective amount of (+)-5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]-2,4-thiazolidinedione (Troglitazone).
8. A method of treating hirsutism, the method comprising administering to a patient suffering from hirsutism a therapeutically effective amount of 5-[p-[1-methylcyclohexyl)methoxy]benzyl]-2,4-thiazolidinedione (Ciglitazone), 5-[p-[2-(5-ethyl-2-pyridyl)ethoxy]benzyl]-2,4-thiazolidinedione (Pioglitazone), 5-[p-[3-(5-methyl-2-phenyl-4-oxazolyl)propionyl]benzyl]-2,4-thiazolidinedione (Darglitazone), or 5-[[[(2R)-2-benzyl-6-chromanyl)methyl]-2,4-thiazolidinedione (Englitazone).
9. A method of treating hirsutism, the method comprising administering to a patient suffering from hirsutism a therapeutically effective amount of 5-(4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl)-2,4-thiazolidinedione (Rosiglitazone).

testosterone, can result in excess **hair** growth.

Because genetics plays a large role in determining how much body **hair** each of us has, "excess" **hair** is a relative term. About 25% of normal women have terminal hairs on the face, around the nipples, or on the lower abdomen, and body **hair** that might be considered unusually heavy in Asian women may be normal among Southern Europeans. However, having more facial or body **hair** than the other women in one's family or experiencing a sudden increase in **hair** may warrant a visit to the doctor to determine whether an underlying disorder is responsible. If other conditions are ruled out, the condition is termed idiopathic hypertrichosis or idiopathic **hirsutism**.

**Medical treatment** Several drugs are effective in treating **hirsutism**. However, **hair** usually regrows once they are discontinued. When **hirsutism** is an effect of polycystic ovary syndrome or insulin resistance, the medications used to treat those conditions often reduce or eliminate the problem. **Metformin**, which increases insulin sensitivity, has had promising results in treating women with both of these related conditions. Oral contraceptives, which help to stabilize hormone balance, are often effective as well.

Gonadotropin-releasing hormone (GnRH) antagonists, such as leuprolide (Lupron), are occasionally used to treat **hirsutism**. These drugs suppress the production of ovarian hormones, thus reducing levels of androgens in circulation. By the same token, they also shut down estrogen production, creating an "artificial menopause" in young women. Estrogen supplementation is also necessary to relieve hot flashes and other menopausal symptoms and to prevent bone loss in women taking GnRH antagonists.

Several drugs developed for other purposes have serendipitously reduced the growth of body **hair**. Finasteride (Proscar), a drug approved to treat prostate enlargement in men, is one of the most promising methods of treating **hirsutism**, as well as **balding**, in women. The drug works by blocking DHT in the skin and scalp. As levels of that hormone drop, follicle stimulation decreases on the face and body, but increases in the scalp. Because the drug's effects are limited to blocking DHT in the target tissues, it doesn't affect levels of estrogen or other hormones in the blood. Although it appears to have few immediate side effects, the consequences of long-term use are unknown.

In studies, spironolactone (Aldactazide), a diuretic, has been as successful as finasteride in treating **hirsutism**, but pharmacologists are uncertain why this is so. Spironolactone is also associated with a number of other effects, including frequent urination and lowered blood pressure. Neither finasteride nor spironolactone should be taken by pregnant women because they may produce genital defects in male fetuses.

Bromocriptine, which is used to treat pituitary conditions that result in prolactin overproduction, has also been associated with a reduction in facial and body **hair**. It is not recommended for women who are pregnant or have just given birth, for people with kidney or liver disease, or for those who have high blood pressure.

There is some evidence that cimetidine (Tagamet)-an acid-blocker for stomach ulcers-and ketoconazole-a systemic antifungal drug-can also reduce **hair** growth. Again, no one is certain why they have this effect. It's important to note that none of these medications is approved by the Food and Drug Administration (FDA) for the treatment of **hirsutism**. Each has side effects that merit careful consideration.

**Hair removal** For most women with excess **hair** that cannot be traced to an underlying medical condition, physical removal is the simplest, easiest, and safest approach. There are a host of products and devices on the market, for both home and professional use. All are subject to varying degrees of federal regulation.

\* **Shaving.** Razors, which are regulated by the Consumer Products Safety Commission, are by far the most common method of **hair** removal worldwide. Contrary to popular belief, shaving merely alters the length of the **hair**-it does not change the texture, color, or rate of **hair** growth.

\* **Depilatories.** These products, be they creams, gels, or lotions, usually contain calcium thioglycolate, an alkaline chemical that breaks down the structure of **hair**, cleaving it off at the surface of the skin. As one might imagine, depilatories don't spare the skin. They often produce minor irritation, and if left on too long, can result in burns. They should be tested on a small area of skin before application and should be used only according to product instructions. They are regulated by the FDA's Office of Cosmetics and Colors. They do not require approval before marketing, but can be taken off the shelves if found to have harmful effects when used as directed.

\* **Tweezing.** This time-honored approach is tedious and can be painful, but presents little risk. Because **hair** is plucked out at the root, it usually takes several weeks to reappear.

\* **Waxes.** These produce longer-lasting results than shaving or depilatories because, like tweezers, they remove the entire **hair** from the follicle. As a result, they are also more painful to use than depilatories. They can be applied at home or in salons. Hot waxes are designed to be heated, applied to the skin in the direction of **hair** growth, and pulled off in the opposite direction, carrying the **hair** with them. Cold waxes are applied in thin strips in the direction of **hair** growth and pulled off against the grain.

Waxes are a brute-force method that can remove skin cells along with **hair**, leaving the skin susceptible to infection. For that reason they should not be used on skin that is cut or irritated; over varicose veins, moles, or warts; inside the nose or ears; or around genital areas. They should be tested on a small area of skin before general application. Like depilatories, they are regulated by the Office of Cosmetics and Colors.

\* **Electrical epilators.** Two types of devices, a needle epilator and a tweezers epilator, are used in a process commonly known as electrolysis. When a needle epilator is used, the operator inserts the fine wire needle into the **hair** follicle close to the **hair** shaft. An electric current travels down the wire and destroys the **hair** root at the bottom of the follicle. When a tweezers epilator is employed, the tweezers grasp the **hair** and the operator sends a current down the **hair** shaft to kill the root.

Both are painstaking procedures that require the individual treatment of each **hair** follicle, and neither is completely effective. The operator may miss the mark or the device may fail to deliver adequate current to the root. Thus, from 15% to 50% of the hairs grow back, and treatment may need to be repeated.

Professional electrologists are licensed in most states. Because needle epilation has been around for longer than a century, it predates the FDA and the devices are therefore not subject to regulation. In 1995, manufacturers of tweezers epilators, which have been in existence for only about 20 years, were asked to submit data on the safety and effectiveness

of their products. The FDA is reviewing the data.

\* Lasers. One type of laser, the ThermoLase Softlight, has received FDA approval for **hair** removal. Its use requires the application of a black-colored solution. After the black pigment penetrates the **hair** follicles, it is washed off the skin. As the laser scans across the area, the pigment in the follicles absorbs the highly focused light, which destroys the **hair** follicles. In clinical trials, the laser eliminated at least 30% of **hair** on the treated areas in 60-70% of patients. Side effects included redness, changes in skin pigmentation, and a risk of scarring.

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